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KERALA STATE DRUG FORMULARY

NUMBER 1
(APRIL 1999)



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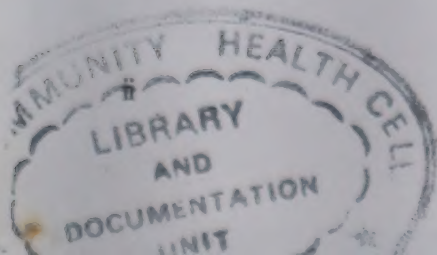
SCOPE

This book is intended for the guidance of medical practitioners, pharmacists, dentists, nurses and others who have the necessary training and experience to interpret the information it provides. It is to be used as a reference and should be supplemented by a study of more detailed publications when required. The guidelines for clinical management at the peripheral hospitals given as Part II of this book are not mandatory. Doctors may use their discretion wherever necessary.

PRICES MENTIONED IN THIS BOOK

Prices for drugs that are marketed in India are given to provide an indication of relative cost of medicines. This is expected to assist the doctor in cost-effective prescribing. Duration of therapy, total cost of therapy and possible advantages should be considered while choosing cost effective drug therapy.

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Foreword

Over the past two decades there has been remarkable changes - both qualitative and quantitative in the scenario of the Health Care system in this country. The advent of modern technology, as applied to medical profession in the form of modern diagnostic gadgets, advances in the novel drug delivery system and facility to disseminate knowledge and information within a second, all contributed to a complex situation where a medical professional has to be necessarily upto date in his techniques and knowledge. Over and above this marketing of more potent and relatively large number of newer drugs, patient's awareness on their right to be informed about the treatment, urge for more transparency in the treatment protocols and procedures are other contributory factors which point to the necessity of providing authentic information on all aspects of drugs to the medical professionals, especially in hospitals where facility for such information is limited and inadequate.

The first part of this book is intended to fulfill the above needs to a large extent. The second part provides essential guidelines for the management of most of the clinical conditions at the hospitals in the periphery. A list of essential drugs to be in stock at such hospitals is also given as part three of the book.

I am sure this book will be of immense help in the utilisation of the available resources for procurement of drugs in the Government hospitals in a better and effective way and thereby will contribute positively in the development of a better Health Care System.

The Committee led by Dr. K.V. Krishna Das has carried out the preparation of this book in a meticulous manner in a limited time and deserves the gratitude of the medical community and the public.

V. VIJAYACHANDRAN
Secretary to Government
Health & Family Welfare Department
Government of Kerala
Thiruvananthapuram

Preface

This drug formulary is the combined effect of a committee nominated by the Government of Kerala and other coopted members. This publication is designed to fulfill the following needs :

1. Give an unbiased and most accepted information on drugs commonly used in practise by doctors at various levels in and outside Government service in Kerala.
2. Give precise prescribing instructions as a ready reckoner for medical officers who may not have immediate access to new literature and peer group consultation.
3. The guidelines formulated for the management of some of the common ailments are designed after common consensus among specialists and members of the health service department with a view to give therapeutic guidelines to doctors working at the periphery and which will also give them ready information for managing clinical problems.
4. The present cost of many of the drugs is included so that the prescribing doctor may use his discretion on quality and cost effectiveness.
5. A suggestion is made regarding the drugs to be made always available at the different level peripheral hospitals in the state so that the drug purchasing authority and medical officers can make use of them if needed.

The task of making a drug formulary is difficult especially so when it has to be need based to suit the public hospitals in the state. This book is not claimed to be encyclopedic in its coverage. What is attempted is description of common and essential drugs needed to treat the vast majority of morbid conditions in Kerala. In the preparation of this drug formulary effectiveness, cost consideration, safety and availability are taken into consideration. Individual doctors may use their discretion in selecting drugs which are not described in this book, depending on their experience and the necessity of the situation.

The production of this book is the result of long and hardwork of the whole team which has interacted on several occasions to complete this volume. Only generic names are used since this is the policy of the WHO as well as the government. It is left to the doctors to select the suitable pharmaceutical preparation.

It was a very enriching and pleasurable experience to interact with the members of this committee. I thank all of them for their prompt action and interaction.

Dr. K.V. Krishnadas.

Chairman

Introduction

Continuing Medical Education programmes, distribution of scientific information leaflets and deliberations at medical conferences play a major role in updating medical officers about scientific and authentic informations on drugs. Such facilities are not accessible to all doctors and the most easily available source of information for many medical officers in various parts of the state is professional interview by the sales personnel of pharmaceutical companies. Information given by pharmaceutical manufacturers are naturally biased by commercial interest and this is inevitable. For proper prescribing, the exact information about drugs and their various aspects is absolutely essential. In India several thousand drug formulations are marketed. Polypharmacy is rampant. Several marketed preparations are shown to be either ineffective or unsatisfactory in quality and notified as such from time to time by the Drugs Controller. It is essential therefore that the prescribing physician has full and correct information about the actions, side-effects, interaction with other drugs and safety at different periods of life in order to make safe and effective prescription. At least 25% of the morbidity in modern clinical practice can be attributed directly or indirectly to drugs. It is therefore absolutely essential that whenever possible monotherapy with specific drugs should be instituted. Drug combination should be resorted to only under proper indications. Several countries including India have formulated lists of essential drugs required to treat the vast majority of illnesses. Drugs in this group are given special importance in this publication.

It is hoped that this publication will serve as a ready-reckoner and guide for our doctors. Constant interaction between the authors and the readers is bound to improve the quality and content and this is what the authors expect.

Chairman
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Convenor
Prof. A.K. Chandrasekharan

How to use the KSDF

Read the Contents, Preface and Introduction, browse through Part I, II, and III

The index provides the name of drugs only. The page number in bold letter indicates the complete detailed monograph of the drug.

Part I of the formulary furnishes the classified notes on drugs.

Part II of the formulary provides suggested guidelines on the management of certain conditions in the peripheral hospitals. These guidelines are not exhaustive and is intended to assist the doctor on duty

Part III of the formulary provides a list of drugs which, in the opinion of the committee, should be available on all occasions in the hospitals.

Abbreviations and Symbols

☆	= essential drugs
b.d.	= two times daily
bw	= body weight
C/I:	= contraindications
CNS	= central nervous system
D/I:	= drug interactions
g	= gram
GI	= gastrointestinal
h	= hourly
h.s.	= at bedtime
hrs	= hours
I:	= indications
i.m.	= intramuscular / intramuscularly
i.v.	= intravenous / intravenously
iu	= international units
kg	= kilogram
L	= litre
max	= maximum
mcg	= microgram
md	= metered dose
mg	= milligram
min	= minute
mL	= millilitre
o.d.	= once daily
P/A:	= dosage forms available
P/C:	= precautions
q.d.s.	= four times daily
s.c.	= subcutaneous / subcutaneously
S/E:	= side effects
t.d.s.	= three times daily

Adverse Drug Reaction

Unwanted or unexpected adverse reaction cannot be ruled out for any drug. Detection and timely reporting of adverse reactions will be of great help in withdrawal of the drug from the market, necessary investigation to identify the underlying factor responsible for the reaction and necessary modification, if possible or banning of the drug for human use.

Doctors are urged to help by reporting adverse reaction to

ADR Monitoring Cell

Kerala State Drug Formulary Unit

College of Pharmaceutical Sciences

Medical College, Thiruvananthapuram - 695011

Adverse Reaction reporting forms are provided as blue coloured cards. Doctors are requested to use the same format.

Doctors are asked to report all suspected reactions (i.e. any adverse or any unexpected event, however minor, which could conceivably be attributed to the drug). Reports should be made despite uncertainty about a causal relationship, irrespective of whether the reaction is well recognized, and even if other drugs have been given concurrently.

Doctors are asked to report all serious suspected reactions, including those that are fatal, life-threatening, disabling, incapacitating, or which result in or prolong hospitalisation; they should be reported even if the effect is well recognised.

Examples include anaphylaxis, blood disorders, endocrine disturbances, effects on fertility, haemorrhage from any site, renal impairment, jaundice, ophthalmic disorders, severe CNS effects, severe skin reactions, reactions in pregnant women, and any drug interactions. Reports of serious adverse reactions are required to enable risk/benefit ratios to be compared with other drugs of a similar class. For established drugs doctors are asked not to report well-known, relatively minor side-effects, such as dry mouth with tricyclic antidepressants, constipation with opioids, or nausea with digoxin.

Special problems

Delayed drug effects

Some reactions (e.g. cancers, chloroquine retinopathy and retroperitoneal fibrosis) may become manifest months or years after exposure. Any suspicion of such an association should be reported.

The elderly

Doctors are asked to be particularly alert to adverse reactions in the elderly.

Congenital abnormalities

When an infant is born with a congenital abnormality or there is a malformed aborted fetus doctors are asked to consider whether this might be an adverse reaction to a drug and to report all drugs (including self-medication) taken during pregnancy.

Vaccines

Doctors are asked to report all suspected reactions to both new and established vaccines. The balance between risks and benefits needs to be kept under continuous review.

Prevention of adverse reactions

Adverse reactions may be prevented as follows :

1. Never use any drug unless there is a good indication. If the patient is pregnant do not use a drug unless the need for it is imperative.
2. It is very important to recognise allergy and idiosyncrasy as causes of adverse drug reactions. Ask if the patient had previous reactions.
3. Ask if the patient is already taking other drugs including self-medication; remember that interactions may occur.
4. Age and hepatic or renal disease may alter the metabolism or excretion of drugs, so that much smaller doses may need to be prescribed. Pharmacogenetic factors may also be responsible for variations in the rate of metabolism, notably of isoniazid and the tricyclic antidepressants.
5. Prescribe as few drugs as possible and give very clear instructions to the elderly or any patient likely to misunderstand complicated instructions.
6. When possible use a familiar drug. With a new drug be particularly alert for adverse reactions or unexpected events.
7. If serious adverse reactions are liable to occur warn the patient.

CONTENTS

Page

PART I: DRUG FORMULARY

CHAPTER 1: General Topics

1.1	Prescription writing	1
1.1.1	Legal requirements about prescription	2
1.2	Patient education	2
1.2.1	Rational drug	2
1.2.2	Importance of educating the patient	3
1.2.3	Patient Education and Litigation	4
1.2.4	Patient education and building rapport	4
1.2.5	Conclusion	4

CHAPTER 2 : Anti infective agents

2.1	Host Parasite Interactions & Pathological consequences of Infection	5
2.1.1	Exotoxins	5
2.1.2	Endotoxins, Macrophages and Cytokines	6
2.1.3	Complements and Neutrophils	6
2.1.4	Platelets and Coagulation	6
2.2	Antimicrobial agents	7
2.2.1	Penicillins	7
2.2.1.1	Benzyl penicillin and its congeners	7
2.2.1.2	Beta lactamase resistant penicillins	9
2.2.1.3	Broad spectrum penicillins	10
2.2.1.4	Extended spectrum penicillins	12
2.2.2	Cephalosporins	13
2.2.2.1	First generation cephalosporins	15
2.2.2.2	Second generation cephalosporins	15
2.2.2.3	Third generation cephalosporins	16
2.2.2.4	Fourth generation cephalosporins	17
2.2.3	Aminoglycosides	17
2.2.4	Tetracyclines	21
2.2.5	Macrolides	23
2.2.6	Chloramphenicol	27
2.2.7	Polyene antibiotics	28
2.2.8	Quinolones	30
2.2.9	Miscellaneous Antimicrobial agents	33
2.2.10	Sulphonamides	37
2.2.11	Drugs used in Leprosy	40
2.2.11.1	National Leprosy Eradication Program Classification	40
2.2.11.2	Treatment objectives	41
2.2.11.3	Treatment of erythema nodosum leprosum (ENL) reaction	41
2.3	Antifungal drugs	41
2.3.1	Classification	41

3.2	Other Topical Antifungals	48
4	Antiviral drugs	48
4.1	Classification	48
5	Antiparasitic agents	53
5.1	Antiprotozoal drugs	53
5.1.1	Antimalarial drugs	53
5.1.2	Other antiprotozoal agents	59
5.1.2.1	Drugs for leishmaniasis	59
5.1.2.2	Drug treatment of amoebiasis	60
5.1.2.3	Drugs for Giardiasis	63
5.1.2.4	Drugs for Trichomoniasis	63
6	Anthelmintics	64
6.1	Choice of drugs for helmenthiasis	68
	Choice of Antimicrobial agents	69

CHAPTER 3 : Drugs used in gastrointestinal disorders

1	Antacids	73
2	Ulcer healing drugs	74
2.1	H ₂ Receptor Antagonists	74
2.2	Proton pump inhibitors	76
2.3	Drugs against Helicobacter pylori (H.Pylori)	77
3	Antispasmodics	79
4	Antiemetics and prokinetics	80
5	Anti diarrhoeals	85
6	Laxatives	87
7	Anti flatulants	91
	Prokinetic drugs	92
9	Antihaemorrhoidal drugs	92
10	Drugs used in inflammatory bowel diseases	93
11	Drugs used in the management of ascites	94
11.1	General approach to administration of drugs in acute and chronic hepatic failure	94
11.2	Drugs used in the management of gall stones	95
13.	Drug Management of haematemesis	440
14	Drugs which lower portal pressure	440
15	Drugs used in primary biliary cirrhosis	440
16	Wilson's disease	440
17	Haemochromatosis	440
18	Drugs used in diseases of the pancreas	95

CHAPTER 4 : Nutrition

	General consideration	96
1	Normal nutrient requirements	96
2	Specific instances where supplemental nutrition should be instituted	101
3	Staple diets	102

4.2	Vitamins	105
4.2.1	Fat soluble vitamins	105
4.2.2	Water soluble vitamins	109
4.3	Mineral Supplementation	115
4.3.1	Nutritional requirement of minerals	116
4.4	Artificial nutritional support	121
4.4.1	Oral diets and nutritional supplements	121
4.4.2	Parenteral nutrition	122

CHAPTER 5 : Drugs used in cardiovascular disorders

5.1	Anti arrhythmic drugs	123
5.1.2	Classification	123
5.1.2.1	Class 1a drugs	123
5.1.2.2	Class 1b drugs	125
5.1.2.3	Class 2 Beta blockers	126
5.1.2.4	Class 3 drugs	126
5.1.2.5	Class 4 Calcium channel blockers	127
5.1.2.6	Positive inotropic agents	127
5.1.2.7	Phosphodiesterase inhibitors	129
5.1.2.8	Sympathomimetic positive inotropic drugs	129
5.2	Drugs used in treatment of angina	131
5.2.1	Nitrates	131
5.2.2	Miscellaneous drugs used in treatment of angina	133
5.3	Drugs used for thrombolytic therapy	134
5.4	Antiplatelet drugs	136
5.5	Anticoagulants	137
5.5.1	Systemic anticoagulants	137
5.5.2	Oral anticoagulants	138
5.6	Lipid lowering drugs	139
5.6.1	Statins	139
5.6.2	Fibric acid derivatives	140
5.6.3	Nicotinic Acid	141
5.7	Antihypertensive drugs	141
5.7.1	Classification of antihypertensive drugs	141
5.7.2	Diuretics	142
5.7.2.1	Thiazide diuretics	142
5.7.2.2	Loop Diuretics	143
5.7.2.3	Potassium Sparing Diuretics	143
5.7.3	Beta Adrenergic Blockers	144
5.7.3.1	Cardioselective betablockers	146
5.7.3.2	Drugs with combined alpha and beta blocker effect	147
5.7.4	Calcium channel blockers	148
5.7.5	Vasodilator drugs	151
5.7.6	Centrally acting antihypertensive drugs	153
5.7.7	Alpha adrenergic receptor blocking agents	154

5.7.8	Drugs affecting the renin angiotensin system (ACE inhibitors)	155
5.7.9	Angiotensin II receptor antagonists	157

CHAPTER 6 : Drugs used in respiratory diseases

6.1	Upper respiratory infections	159
6.1.1	Common cold (Rhinitis)	159
6.1.1.1	Topical Nasal Decongestants	159
6.1.1.2	Antihistamine	159
6.1.1.3	Sodium chloride	160
6.1.1.4	Sympathomimetics	160
6.1.2	Allergic rhinitis and nasobroncheal allergy	161
6.1.2.1	Mast cell stabilizers	161
6.1.2.2	Corticosteroids	161
6.1.2.3	Oral Antihistamines	162
6.2	Drugs used in tuberculosis	165
6.2.1	RNTCP treatment regimen	168
6.2.2	Reserve drugs	169
6.3	Drugs used in the treatment of airway diseases	172
6.3.1	Asthma and chronic obstructive pulmonary disease (COPD)	172
6.3.1.1	Bronchodilators (Beta 2 adrenergic agonists)	172
6.3.1.2	Anticholinergics	174
6.3.1.3	Systemic steroids	175
6.3.1.4	Inhaled Steroids	176
6.3.1.5	Mast Cell stabilizers	177
6.3.1.6	Leucotriene receptor antagonist	179
6.3.1.7	5 - lipo oxygenase inhibitor	179
6.3.1.8	Antigens for immunotherapy	179
6.3.2	Newer drug delivery systems in asthma	179
6.4	Respiratory stimulants	180
6.5	Cough suppressants (Antitussives)	182
6.6	Expectorants	183
6.7	Mucolytics	184
6.8	Pulmonary surfactant	184
6.9	Oxygen therapy	185
6.10	Haemostatics	187
6.11	Anticoagulants	188
6.11.1	Heparin	188
6.11.2	Oral anticoagulants	188

CHAPTER 7 : Drugs used in endocrine disorders

7.1	Disorders of glucose metabolism	189
7.1.1	Drugs used in diabetes mellitus	189
7.1.1.1	Oral hypoglycemic agents	190
7.1.1.1.1	Sulphonyl ureas	190
7.1.1.1.2	Biguanides	192
7.1.1.2	Guargum	193

7.1.1.3	Acarbose	193
7.1.1.4	Insulins	194
7.1.2	Drugs used in gestational diabetes	197
7.1.3	Drugs used in acute myocardial infarction for control of diabetes.	197
7.1.4	Diabetic nephropathy	197
7.1.5	Diabetic neuropathy	197
7.1.6	Drugs precipitating or aggravating diabetes	198
7.1.7	Drugs that raise blood sugar in acute hypoglycemia	198
7.2	Drugs acting at hypothalamus and pituitary	198
7.2.1	Drugs acting at hypothalamus	198
7.2.2	Drugs acting at pituitary	201
7.2.2.1	Anterior pituitary hormones	201
7.2.2.2	Posterior pituitary hormones	203
7.3	Drugs for thyroid disorders	205
7.3.1	Management of hypothyroidism	205
7.3.2	Drugs used for hyperthyroidism	206
7.3.3	Drugs used in treatment of thyroid cancers	209
7.4	Diseases of the parathyroid	209
7.5	Adrenal hormones	213
7.5.1	Replacement therapy for adrenocortical insufficiency	214
7.5.2	Adrenal crisis	215
7.5.3	Cushing's syndrome	215
7.5.4	Congenital adrenal hyperplasia	215
7.6	Sex hormones	216
7.6.1	Female sex hormones	217
7.6.1.1	Oestrogens	217
7.6.1.2	Progestogens	219
7.6.2	Male sex hormones	221
7.6.3	Antiandrogens	222
7.6.4	Anabolic steroids	223
CHAPTER 8 : Analgesics and antiinflammatory agents		
8.1	Analgesics	225
8.1.1	Non-opioid analgesics	225
8.1.2	Opioid analgesics	227
8.1.3	Drugs for trigeminal neuralgia	233
8.1.4	Drugs for migraine	233
8.2	Drugs used in the treatment of musculoskeletal and joint disorders	236
8.2.1	Non-steroidal anti-inflammatory drugs	236
8.2.2	Corticosteroids	242
8.2.3	Drugs which suppress the rheumatic disease process	243
8.2.4	Drugs for treatment of gout	248
8.2.5	Drugs for the relief of soft tissue inflammation	250
8.2.6	Rubefacients and other topical counter irritants	251

CHAPTER 9 : Drugs acting on blood and blood forming organs	
9.1	Nutritional anaemias 252
9.1.1	Iron deficiency anaemia 252
9.1.2	Megaloblastic anaemia 252
9.2	Haemolytic anaemias 252
9.2.1	Acquired haemolytic anaemias 252
	Autoimmune haemolytic anaemia 252
9.2.2	Drug induced haemolytic anaemia 254
9.2.3	Haemolytic disease of the newborn 254
9.2.4	Symptomatic haemolytic anaemias 255
9.2.5	Paroxysmal nocturnal haemoglobinuria 255
9.2.6	Inherited enzyme deficiencies leading to haemolytic anaemias 255
9.3	Hypoplastic and aplastic anaemia 255
9.3.1	Anabolic steroids 256
9.3.2	Immunosuppressants 256
9.4	Haemoglobinopathies 257
9.4.1	Sickle cell anaemia 257
9.4.2	Sickle cell trait 258
9.4.3	Thalassemias 258
9.4.3.1	Heterozygous thalassemia (thalassemia minor) 259
9.4.3.2	Thalassemia syndromes 259
9.5	Iron chelating drugs 259
9.6	Drugs used in leukaemia 260
9.6.1	Chronic myeloid leukaemia 260
9.6.2	Chronic lymphatic leukaemia 263
9.6.3	Acute leukaemia 263
9.6.4	Myelodysplastic syndrome 264
9.6.4.1	Haematopoietic growth factors 265
9.6.5	Multiple myeloma 265
9.6.6	Lymphomas 266
9.6.6.1	Hodgkin's disease (Hodgkin's lymphoma) 266
9.6.6.2	Non-Hodgkin's Lymphoma 266
9.7	Drugs used in the treatment of haemorrhagic disorders 267
9.7.1	Purpuras 267
9.7.1.1	Acute ITP 267
9.7.1.2	Chronic ITP 268
9.7.1.3	Henoch schonle in purpura (vascular purpura) 269
9.7.2	Thrombopathy 269
9.8	Coagulation defects and their management 269
9.8.1	Haemophilia and other coagulopathies 269
9.8.2	Fibrinogen deficiency 270
9.9	Antiplatelet drugs 271
9.10	Anticoagulants 271
9.10.1	Heparin 272
9.10.2	Oral anticoagulants 273

9.10.2.1	Drugs which enhance anticoagulant effects	274
9.10.2.2	Drugs which impair the anticoagulant action	274
9.10.2.3	Antidote to oral anticoagulants	275
9.11	Antifibrinolytic drugs	275
9.12	Thrombolytic agents	276

CHAPTER 10 : Drugs used in neurological disorders

10.1.	Drugs which enhance neuromuscular transmission	278
10.1.1	Anticholinesterases	278
10.1.2	Skeletal muscle relaxants	279
10.1.3	Other muscle relaxants	280
10.2	Antiepileptics	281
10.2.1	Drugs used in status epilepticus	290
10.2.2	Febrile convulsions	291
10.3	Drugs used in parkinsonism and other movement disorders	291
10.3.1	Dopaminergic drugs used in parkinsonism	292
10.3.2	Antimuscarinic drugs used in parkinsonism	296
10.4	Drugs used in essential tremor, chorea, tics and related disorders	298
10.5	Drugs used in nausea and vertigo	298

CHAPTER 11 : Drugs used in psychiatry

11.1.	Antipsychotics	305
11.1.1	Phenothiazines	305
11.1.2.	Thioxanthines	309
11.1.3	Butyrophenones	309
11.1.4	Dibenzoxazepines	310
11.1.5	Diphenyl butylpiperidines	310
11.1.6	Benzisoxazole	311
11.1.7	Dibenzodiazepine	311
11.2	Antidepressants	312
11.2.1.	Tricyclic antidepressants	313
11.2.2	Serotonin-specific reuptake inhibitors	317
11.3	Mood stabilizers	318
11.3.1	Lithium carbonate	318
11.3.2.	Iminostilbenes	319
11.3.3	Valproic acid derivatives	319
11.3.4.	Calcium channel blockers	319
11.4.	Anxiolytics	319
11.4.1	Benzodiazepines	319
11.4.2	Buspirone hydrochloride	322
11.5	Sedatives and hypnotics	322
11.5.1	Benzodiazepines	323
11.5.2	Chloral and derivatives	323
11.5.3	Non-benzodiazepine	324

1.5.4	Antihistamines active primarily on the CNS	325
1.6.	Drugs used in substance use disorders	325
1.6.1	Alcohol abuse	326
1.6.2.	Opioid abuse	326
1.7	Drugs used in drug induced movement disorders	327
1.7.1	Anticholinergics	327
1.7.2	Amantidine	327
1.7.3	Propranalol	327
1.8	Cerebral stimulants	327

CHAPTER 12: Drugs used in diseases of kidney and urinary tract

2.1	Diuretics	330
2.1.1	Thiazide diuretics	330
2.1.2	Loop diuretics	333
2.1.3	Potassium sparing diuretics	335
2.1.4	Osmotic diuretics	336
2.1.5	Carbonic anhydrase Inhibitors	336
2.2	Immunosuppressive therapy	336
2.3	Drug treatment of urolithiasis	340
2.3.1	Drug therapy	340
2.3.2	Chelating agents used in the treatment of cystine stones	342
2.4	Treatment of voiding dysfunction and other common lower urinary problems	342
2.4.1	Drugs for Benign prostatic hypertrophy (BPH)	342
2.4.2	Treatment of neurogenic voiding dysfunction	343
2.4.3	Drugs for urinary frequency and enuresis	343
2.4.4	Drugs used in Nocturnal enuresis	344
2.4.5	Alkalinisation of urine	344
2.4.6	Acidification of urine	344
2.5	Nephrotoxic drugs	344
2.5.1	Commonly encountered drug nephrotoxicity	345
2.5.2	Drug dose modification in renal failure	348

CHAPTER 13: Anaesthetic agents

1	Drugs used for general anaesthesia	350
1.1	Intravenous anaesthetics	350
1.2	Inhalational agents	352
1.3	Gaseous agents	354
1.4	Premedicants	354
1.5	Muscle relaxants	356
2	Local anaesthetics	358
2.1	Sodium channel blockers	358
2.2	Miscellaneous local anaesthetics	359

CHAPTER 14: Drugs used in dermatology

1	Superficial bacterial infections	360
1.1	Topical therapy	360

14.1.2	Systemic therapy	362
14.2	Superficial and deep mycoses	365
14.2.1	Topical therapy	365
14.2.2	Systemic therapy	369
14.3	Viral infection	370
14.3.1	Warts	370
14.3.2	Molluscum contagiosum	370
14.3.3	Herpes simplex	370
14.3.4	Herpes genitalis	370
14.3.5	Herpes zoster	371
14.4	Psoriasis	371
14.4.1	Local therapy	371
14.4.2	Systemic therapy	373
14.5	Eczemas	375
14.5.1	Topical therapy	375
14.5.2	Systemic therapy	375
14.6	Pemphigus	375
14.7	Toxic epidermal necrolysis	376
14.8	Dermatitis herpetiformis	376
14.9	Erythema multiforme, Steven Johnson's Syndrome	376
14.10	Urticaria, Angioedema	376
14.11	Fixed drug eruption	376
14.12	Lichen planus	376
14.13	Pityriasis rosea	377
14.14	Acne vulgaris	377
14.14.1	Topical therapy	377
14.14.2	Systemic therapy	378
14.15	Hypopigmentation	378
14.16	Hyperpigmentation	378
14.17	Alopecia	378
14.18	Pediculosis	379
14.19	Scabies	379
14.20	Melanoma	381
14.21	Antiperspirants	381
14.22	Material for wound dressings	381
14.23	Astringents	381
CHAPTER 15 : Drugs used in paediatric practice		
15.1	Prescribing for children	382
15.1.1	Antibacterials	383
15.1.2	Anthelmintics	387
15.1.3	Antiprotozoal agents	388
15.1.4	Antituberculosis drugs	389
15.1.5	Antipyretic analgesics	390
15.1.6	Antispasmodics	391
15.1.7	Antihistaminics/antiemetics	391
15.1.8	Bronchodilators	393

15.1.9	Prophylaxis of asthma	394
15.1.10	Anticonvulsants	395
15.1.11	Sedatives	396
15.1.12	Cardiovascular drugs / antihypertensives	397

CHAPTER 16 : Gynaecology

16.1	Nutritional requirement in pregnancy	399
16.1.1	Ideal diet prescribed for antenatal woman	399
16.2	Drugs and pregnancy	399
16.2.1	Drugs to be avoided in 1st trimester	400
16.2.2	Drugs which are possibly teratogenic and better avoided in pregnancy unless absolutely indicated	400
16.2.3	Drugs to be avoided in 3rd trimester as far as possible	400
16.2.4	Drugs contra indicated in lactation	400
16.3	Dos and don't in pregnancy	400
16.3.1	Confirmation of pregnancy	400
16.3.2	Pattern of antenatal visits	400
16.3.3	What should be done at each visit	400
16.3.4	Basic investigations to be done	401
16.4	Oxytocics	401
16.4.1	Induction of labour	403
16.4.2	Induction of abortion (MTP)	404
16.5	Vaginitis	404
16.5.1	Monilial vaginitis	404
16.5.2	Trichomonas vaginalis vaginitis	405
16.5.3	Atrophic vaginitis	405
16.6	Contraceptives	405
16.6.1	Oral contraceptives	405
16.6.2	Injectable contraceptives	405
16.6.3	Emergency contraception	406
16.7	Drugs used for induction of ovulation	406

CHAPTER 17: Antineoplastic agents

17.1	Alkylating Agents	407
17.2	Antimetabolites	411
17.3	Vinca alkaloids	413
17.4	Cytotoxic antibiotics	414
17.5	Hormones and hormonal antagonists	417
17.6	Miscellaneous Agents	420

CHAPTER 18 : Drugs used in ENT infections

18.1	Topical medication used in ENT Practice	421
18.1.1	Nasal preparation	421
18.1.1.1	Local sympathomimetic decongestants	421
18.1.1.2	Corticosteroid nasal spray	422
18.1.1.3	Mast cell stabilizers	422
18.1.2	Aural preparations	422

18.1.2.1	Antibacterials	422
18.1.2.2	Corticosteroids	423
18.1.2.3	Antifungals	424
18.1.2.4	Ceruminolytics	424
18.1.3	Oropharyngeal preparations	424
18.1.3.1	Anti inflammatory analgesics	424
18.1.3.2	Antibacterials	424
18.1.3.3	Antifungal preparations	425
18.2	Systemic antihistamines	425

CHAPTER 19 :Drugs used in ophthalmology

19.1	Routes of administration of drug	431
19.2	Antibacterial agents	432
19.3	Antiviral agents	432
19.4	Antifungal agents	433
19.5	Local anaesthetics	434
19.6	Drugs used in medical management of glaucoma	434
19.6.1	Cholinergic drugs used topically	434
19.6.2	Adrenergic drugs	435
19.6.3	Systemic drugs used in glaucoma	436
19.7	Corticosteroids used in ophthalmology	436
19.8	Mydriatics, miotics and cycloplegic drugs	437
19.9	Dyes used in ophthalmology	439
19.10	Nutritional disorders affecting the eye	439

PART II : GUIDELINES FOR CLINICAL MANAGEMENT AT THE PERIPHERAL HOSPITALS

1.	General conditions	442 - 444
1.1	Hyperpyrexia	442
1.2	Enteric fever	442
1.3	Acute anaphylactic reactions	442
1.4	Prevention and treatment of penicillin reactions	442
2.	Nutritional disorders	444
3.	Toxicology and envenomation	444 - 454
3.1	Toxicology	444
3.1.1	General management of the poisoned patient	444
3.2	Envenomation	450
3.2.1	Snake envenomation	450
3.2.2	Bee and wasp stings	453
4.	Paediatrics	454 - 462
4.1	Diarrhoea and Dehydration	454
4.2	Acute lower respiratory tract infections (LRTI)	455
4.3	Acute Severe Asthma (in children)	457
4.4	Staphylococcal pneumonia	458

4.5	Pyogenic Meningitis	458
4.6	Primary tuberculosis (in children)	459
4.7	Resuscitation of Newborn	459
4.8	Poisoning in children	460
4.8.1	Some common poisoning in children and their management	461
5.	Immunisation	462 - 483
5.1	Active Immunisation	462
5.2	Passive Immunisation	462
5.3	Common side effects to vaccine and their management	463
5.4	Vaccines mandatory for all children	465
5.4.1	BCG Vaccine (Bacillus Calmette Guerin)	466
5.4.2	Poliomyelitis Vaccine	466
5.4.3	Measles Vaccine	467
5.4.4	Triple Antigen (Diphtheria , Pertussis, Tetanus) (DPT Vaccine)	467
5.4.5	Double Antigen (DT)	468
5.4.6	Tetanus Toxoid (TT)	468
5.5	Optional vaccines	469
5.5.1	Mumps, Measles & Rubella (MMR)	469
5.5.2	Rubella Vaccine	470
5.5.3	Hepatitis B Vaccine (HB)	470
5.5.4	Typhoid Vaccine	472
5.5.5	Haemophilus Influenza Type b Conjugate Vaccine (Hib Vaccine)	472
5.6	Vaccines for specific purpose	473
5.6.1	Rabies Vaccine	473
5.6.2	Cholera Vaccine	474
5.6.3	Yellow Fever Vaccine	474
5.6.4	Meningococcal Vaccine	474
5.6.5	Pneumococcal Vaccine	475
5.6.6	Japanese B Encephalitis Vaccine	475
5.6.7	Hepatitis A Vaccine	475
5.6.8	Varicella Vaccine	475
5.6.9	Influenza Vaccine	476
5.7	Antisera used for passive immunisation	476
5.7.1	Diphtheria Antitoxin. (Antidiphtheric serum)	476
5.7.2	Gas Gangrene Antitoxin (anti gas gangrene serum) AGGS	477
5.7.3	Tetanus Antitoxin (Anti tetanus serum) ATS	477
5.7.4	Normal Human Immunoglobulin(Ig)	478
5.7.5	Intravenous gammaglobulin	478
5.7.6	Anti D(RhD) Immunoglobulin	479
5.8	Cold Chain	479
5.8.1	Subcentre level	479
5.8.2	PHC level	481

8.9	Near Drowning	504
5.8.3	District store level	482
6.	Gastroenterology	483 - 484
6.1	Jaundice	483
6.2	Haematemesis	483
6.3	Gall stones	484
7.	Cardiology	484 - 500
7.1	Cardiac arrest	484
7.2	Acute myocardial infarction	486
7.3	Cardiac tamponade	487
7.4	Acute cardiogenic pulmonary oedema	487
7.5	Acute pulmonary embolism	488
7.6	Chest pain	489
7.7	Common arrhythmias	489
7.7.1	Bradyarrhythmias	489
7.7.2	Tachyarrhythmias	490
7.7.2.1	Narrow QRS complex tachycardia.	490
7.7.2.2	Wide QRS complex tachycardia	491
7.8	Congestive cardiac failure	492
7.9	Hypertensive crisis	493
7.10	Hypertension	494
7.11	Secondary hypertension	497
7.12	Angina Pectoris	498
7.13	Hypotension	499
7.14	Infective Endocarditis	499
8.	Respiratory system	500 - 507
8.1	Community Acquired Pneumonia	500
8.2	Hospital Acquired Pneumonia	500
8.3	Acute severe asthma	500
8.4	Chronic asthma in adults	501
8.5	Asthma in children < 5 Years of age	502
8.6	Chronic Obstructive Pulmonary Disease	502
8.7	Respiratory failure	503
8.8	Pulmonary embolism	503
8.10	Foreign Body aspiration and acute pulmonary collapse	504
8.11	Pulmonary aspiration	504
8.12	Inhalation of toxic gases	505
8.13	Haemoptysis	505
8.14	Acute respiratory distress syndrome (ARDS)	506
8.15	Tension pneumothorax	506
8.16	Pleural effusion	507
9.	Neurology	507 - 522
9.1	Meningitis	507
9.1.1	Bacterial meningitis prior to hospitalisation	507

9.1.1.1	Causative organism or susceptibility not yet known	508
9.1.1.2	Causative organism of known identity and susceptibility	508
9.1.2	Hospital-acquired meningitis	509
9.2	Pyogenic meningitis in adults	509
9.3	Tuberculous Meningitis	510
9.4	Epilepsy	510
9.5	Status epilepticus	512
9.6	Coma	513
9.7	Central Nervous System tuberculosis	513
9.8	Cerebral Malaria	514
9.9	Herpes Simplex Encephalitis	514
9.10	Brain Abscess or Subdural Empyema	514
9.11	Toxoplasma Encephalitis/Abscess	515
9.12	Neurosyphilis	515
9.13	Cerebrovascular occlusive disease	515
9.14	Cerebral Oedema and Raised Intracranial Pressure	516
9.15	Raised intracranial tension	517
9.16	Intracranial haemorrhage	520
9.17	Subarachnoid Haemorrhage	520
9.18	Bell's Palsy	520
9.19	Guillain -Barre Syndrome	520
9.20	Migraine	521
10.	Nephrology	522 - 529
10.1	Acute renal failure	522
10.2	Acute glomerulonephritis (AGN)	524
10.3	Urinary tract infections	524
10.3.1	Infections of the lower urinary tract	525
10.3.2	Infections of the upper urinary tract	526
10.4	Prostatitis	527
10.5	Chronic bacterial prostatitis	527
10.6	Chronic renal failure (CRF)	527
10.7	Renal cortical abscess (renal carbuncle)	529
10.8	Infected renal cysts	529
10.9	Perinephric abscess	529
10.10	Urethral syndrome	529
11.	Haematology	529 - 534
11.1	Nutritional Anaemia	529
11.2	Haemorrhagic Disorders	530
11.3	Blood and blood component therapy	530
12.	Endocrinology	534- 536
12.1	Diabetes mellitus	534
12.2	Diabetic ketoacidosis	535
12.3	Hypoglycemia	535
12.4	Thyroid storm	535
12.5	Myxoedema coma	536
12.6	Adrenal crisis	536
12.7	Hypercalcemia	536
13.	Obstetrics and gynaecology	537 - 541

13.1	Hyperemesis Gravidarum	537
13.2	Ectopic gestation	537
13.3	Antepartum haemorrhage	537
13.4	Eclampsia	538
13.5	Preterm Labour	538
13.6	Pre labour Rupture of Membranes	539
13.7	Postpartum haemorrhage	539
13.8	Hypertension in Pregnancy	540
13.9	Diabetes in pregnancy	540
14.	Cancer and palliative medicine	541
14.1	Cancer pain(WHO guidelines)	541
15.	Ear, nose and throat	542 - 545
15.1	Epistaxis	542
15.2	Acute laryngeal oedema due to allergic angioedema	544
15.3	Acute tonsillitis	543
15.4	Chronic tonsillitis	543
15.5	Acute sinusitis	543
15.6	Chronic sinusitis	543
15.7	Infections of the external ear	544
15.8	Infection of middle ear	544
15.9	Infection of nose and paranasal sinus	544
15.10	Infection of oropharynx	545
15.11	Principles in the choice of antibiotics for ENT diseases	545
16.	Ophthalmology	545 - 546
16.1	Foreign body in the eye	545
16.2	Conjunctivitis	545
16.3	Chemical burn	545
16.4	Iridocyclitis or Uveitis	546
16.5	Recognition of refractive error in child	546
16.6	Identification of cataract for surgery	546

**PART III: SUGGESTED LIST OF DRUGS TO BE
IN STOCK AT ALL THE TIMES IN THE
GOVERNMENT HOSPITALS**

547-554

APPENDIX - I	Schedule G Drugs	555
APPENDIX- II	Schedule H Drugs	557
APPENDIX - III	Schedule X Drugs	562
APPENDIX - IV	Banned Drugs	563
APPENDIX - V	Dental Practitioners Formulary	566
APPENDIX - VI	National Essential Drug List	568
APPENDIX - VII	Pregnancy Risk Category of Drugs	575

INDEX

583-601

PART - I

Drug Formulary

CHAPTER 1: GENERAL TOPICS

1.1 PRESCRIPTION WRITING

Medicines are to be prescribed only when they are absolutely necessary and in all cases the relative benefit of administering the drug and the risk involved should be evaluated.

While prescribing, the guidelines given below may be followed:

1. Prescription should be written in ink or otherwise so as to be indelible.
2. Full name and address, age and sex of the patient should be stated on the prescription.
3. All prescription should be dated.
4. The generic name of the drug should be used unless bioavailability problems are important and in such cases the proprietary name or the name of the manufacturer may also be indicated.
5. The strength and quantity to be contained in capsules, tablets, etc. should be stated, if the drug is available in different strength.
6. Avoid unnecessary use of decimal point, eg. 3 mg, *not* 3.0 mg
7. Quantities less than 1 mg should be written in micrograms, eg. 100 microgram, *not* 0.1mg
8. When decimals are unavoidable a zero should be written in front of the decimal point when there is no other figure, eg. 0.5 mL, *not* .5 mL.
9. Micrograms and nanograms should not be abbreviated.
10. The term 'millilitre' (ml or mL) should be used and cubic centimetre or cc should not be used.
11. Dose and dose frequency should be stated and in the case of preparations to be taken 'as required', a minimum dose interval should be specified.
12. The quantity to be supplied may be stated for each drug in a prescription.
13. Directions to the patient should be written in Malayalam or English without abbreviations. However if necessary, some latin abbreviations which are widely prevalent may also be used.
14. The signature, name and address of the prescriber should be present in a prescription.

1.1.1 Legal requirements about prescription

The legal responsibility for a prescription lies with the doctor who signs the prescription.

1. Drugs included in the Schedule G (see appendix-I) of the Drugs and Cosmetic Act 1945 and Rules should be administered only under the supervision of a Registered Medical Practitioner.
2. Drugs included in the Schedule H (see appendix-II) of the Drug and Cosmetic Act 1945 and Rules should be dispensed only on the prescription of a Registered Medical Practitioner.
3. Drugs included in the Schedule X (see appendix-III) of the Drugs and Cosmetic Act 1945 and Rules are psychotropic drugs and all prescription for such drug should be made in duplicate and the full signature, name, Registration number in the State Medical Council and address of the prescriber is mandatory.

1.2 PATIENT EDUCATION

1.2.1 Rational drug use is a new concept so much debated at various levels. It can be defined in 6 'R's.

- ♦ Right choice of drug
- ♦ Right time.
- ♦ Right dose
- ♦ Right intervals
- ♦ Right length of time.
- ♦ Right cost.

It has following dimensions.

- a. Learn about the clinical pharmacology of drugs.
- b. Prescribe the drug rationally.
- c. Devise a plan for monitoring the actions of drug - both beneficial and harmful - and to determine the end point for therapy
- d. Plan a programme for patient education

1.2.2 Importance of educating the patient

Patient compliance

Man is a rational animal and he should be clearly convinced about the importance of proper drug use in relation to the disease. There is always the risk of noncompliance and treatment failures particularly in our socio-cultural set up where a lot of people give all sorts of advice and comments about the utility and potential side effects of drugs (real as well as alleged). The diagnosis and reasoning underlying it should be shared with the patient in appropriate level and amount. The prescriber should describe to the patients and his relatives all aspects of drug use including the kind of drug effect which should be monitored and in what way including laboratory tests and signs and symptoms that the patient should report.

Titrating the optimal dosage and duration of therapy

In diseases where the therapeutic dose is to be individualised by trial and error (as in epilepsy or hypertensive) unless the patient is educated properly, cooperation cannot be achieved. For conditions that call for limited course of therapy, duration of therapy should be made clear so that patient should not stop taking drug prematurely. In case of prolonged therapy, perhaps indefinite as in rheumatoid arthritis the need for prolonged therapy should be stressed. Any change in patient's condition that demand alteration in therapy should be specified.

Monitoring for adverse effect

Unless the patient is aware of potential side effects, early detection and reporting of toxicity symptoms may not be possible. Major toxicity that require immediate alteration and sometimes withdrawal of drug should be clearly explained to the patient.

Ensuring proper non-drug factors involved in drug therapy

Apart from the chemical nature of drug, more important will be the various factors influencing absorption and metabolism.
eg. Rifampicin to be taken atleast 2 hours before food.

To avoid self medication

The drugs prescribed once may be used later on by many patients without consultation on the basis of more or less similar

symptomatology. This practice of self medication should be avoided by proper patient education by highlighting the possibility for toxic effects.

1.2.3 Patient Education and Litigation

In the present socio cultural situations of consumer protection act, proper instruction to the patients about potential side effects is absolutely essential and this fact should be recorded and his consensus obtained.

1.2.4 Patient education and building rapport

Time and effort spent in interacting with the patient during education and motivation is really an investment for developing better rapport and better "doctor-patient" relationship.

1.3 CONCLUSION

Patient education is an integral part of treatment. Prescription writing forms only a minor part in the art and science of medical practice. The prescriber and his health care team should be ready to repeat and extend the information transmitted to the patient as often as possible. The more toxic the drug prescribed and more prolonged the course of treatment, greater is the importance of the education programme.

CHAPTER 2 : ANTI INFECTIVE AGENTS

2.1 HOST PARASITE INTERACTIONS & PATHOLOGICAL CONSEQUENCES OF INFECTION

Infection involves complicated interactions of parasite and host and inevitably affects both.

Surface contact

Most often, the first contact between host and parasite is at a mucosal or cutaneous surface. Mechanical barriers, for example, including the skin and flow of secretions from glands tend to prevent infection by any potential pathogen. The normal commensal microflora, present on mucosal surfaces prevent invasion by pathogens.

Organism specific immune system that functions at mucosal surfaces include specialized macrophages of lymphocytes. This mucosa associated lymphoid tissue traps antigens. Further elaboration of secretory IgA prevents adherence and penetration by organisms.

Invasion

Microorganisms attached to a mucosal surface use specific mechanisms to invade deeper host structures. Meningococci and gonococci penetrate and traverse mucosal epithelial cells by transcytotic mechanism. Salmonellae induce their own phagocytosis by the host's gastrointestinal macrophages. Bacteria then resist killing by the phagolysosome of the unactivated macrophages. Several other pathogens enlist the aid of insect vectors to break the protective skin and enter the tissues.

Microbial Virulence Strategies

Microbes have developed a variety of strategies for escaping host immunity. Many bacteria are encapsulated with polysaccharide that allow them to evade complement deposition in the absence of specific antibodies.

2.1.1 Exotoxins

A common and serious cause of tissue damage, especially in bacterial infection, is the active secretion of 'exotoxins' by the parasite.

Most of the exotoxins are proteins. Toxins are generally more highly conserved in their structure than the surface antigens of the organism secreting them. Exotoxins help to develop cross immunity between microbes.

Bacterial products promoting survival and spread of bacteria. Examples include hyaluronidase, collagenase, DNAase and streptokinase. Some staphylococci release a coagulase which deposits

a protective layer of fibrins onto and around the cells, thus localizing them.

B. Toxins damaging and destroying cells.

Cell membranes can be damaged enzymatically by lecithinases or phospholipases or by insertion of pore forming molecules that destroy the integrity of the cells.

C. Toxins interfering with cell metabolism.

Several toxins enter cells and actively alter some of their metabolic machinery.

eg. diphtheria and cholera toxin.

D. Toxins affecting passage of nerve impulses.

eg. toxins of tetanus and botulinum toxin.

2.1.2 Endotoxins, Macrophages and Cytokines

Endotoxins are integral parts of microbial cell wall and these are characteristic of gram -ve bacteria. They are typically lipopolysaccharides (LPS) composed of a lipid portion (lipid A) inserted into the cell wall, a conserved core polysaccharide and a highly variable O- polysaccharide responsible for the serological diversity which is a feature of organisms like salmonella and shigella. The most important effects of LPS are fever and vascular collapse or shock. IL - 1 and TNF (Tumour Necrosis Factor) are produced by macrophages in response to LPS. Bacteria like salmonella, shigella, E.coli and meningococci produce cytokines like IL-1 and TNF. Staph. aureus and mycobacteria also produce TNF.

Endotoxic or septic shock is usually associated with systemic spread of organisms eg: gram -ve septicemia due to E.coli, N.meningitidis etc. In shock the intestinal mucosa loses its barrier function and therefore organisms freely get into the system.

2.1.3 Complements and Neutrophils

Direct activation of complement by LPS may contribute to shock : C3a and C5a are produced in large amounts and there is leucopenia. Activation of polymorphonuclear cells release oxidative and nonoxidative molecules and produces shock. Changes in the pulmonary capillaries may result in adult respiratory distress syndrome (ARDS).

2.1.4 Platelets and Coagulation

Disseminated intravascular coagulation (DIC) can result from bacterial septicemia, viral infection like dengue and others.

Even now infectious diseases remain a major problem and constitute about a third of the total morbidity despite several advances in the diagnosis and treatment. Though many antimicrobial agents have been introduced and put to clinical use from time to time, the microbial pathogens have not been

totally controlled due to their capacity to develop resistance to the drugs. It is therefore very important that the clinician must have clear guidelines in selecting the appropriate antimicrobial agent and to get the desired effect so as to ensure that the drug is used in full dose for the optimum period of time.

2.2 ANTIMICROBIAL AGENTS

2.2.1 Penicillins

The present antibiotic era was ushered in with the commercial availability of penicillins. This was the first antibiotic introduced clinically. It is a betalactam antibiotic. The basic nucleus of penicillin is 6-aminopenicillanic acid which contains a thiazolidine ring linked to betalactam ring. Penicillins are bactericidal and interfere with synthesis of bacterial cell wall peptidoglycan.

Penicillin Resistance:

This may be due to

1. Production of betalactamases, mainly by staphylococci, gonococci and haemophilus. Resistance due to this enzyme is overcome by concomitant use of a betalactamase inhibitor like clavulanic acid, sulbactam, tazobactam.
2. Reduction in the permeability of outer membrane. Mainly occurs in gram negative organisms which have an outer membrane which limits the penetration of hydrophilic antibiotics.
3. Occurrence of modified penicillin binding sites. Even though some penicillins (eg. methicillin) are not significantly inactivated by betalactamases, they are not active against some staphylococci. This is due to alteration in the binding sites for betalactams.

The presence of proteins or other constituents of pus, low pH or low oxygen tension does not appreciably decrease the ability of betalactams to kill the bacteria. However bacteria that survive inside viable cells of the host are protected from the action of betalactam antibiotics.

Classification of Penicillins

2.2.1.1 Benzyl penicillin and its congeners ☆

They are : Benzyl penicillin (Penicillin G)
Phenoxymethyl penicillin (Penicillin V)
Procaine penicillin
Benzathine penicillin

They are highly effective against gram positive cocci, but they are hydrolysed

by penicillinase and therefore, ineffective against staphylococci. Penicillin G has to be given preferably by parenteral route since only about 30 % of the drug is absorbed and the rest is inactivated by the acidic gastric secretion. Penicillin V can be given orally. Food interferes with the absorption of penicillin V. So it should be given orally at least 30 minutes before or 2 - 3 hours after a meal.

- I: Infections by the following susceptible organisms - S.haemolyticus, pneumococcus, susceptible or non resistant gonococci, meningococci, spirochetes such as T.pallidum, T.pertenuis, leptospira, anaerobes such as C.tetani, C.botulinum, C.perferingens, peptococcus, peptostreptococcus, bacteroids, anthrax, and others. Staphylococci which are susceptible to penicillin respond well to this antibiotic.

The clinical indications include acute tonsillitis, upper respiratory tract infection, pneumonia, gonorrhoea, meningococcal and pneumococcal meningitis, syphilis, yaws, anaerobic and mixed infections and others.

- C/I: Absolute contraindication - any history or even doubtful hypersensitivity to penicillin.

Exposure to even test doses should be avoided since penicillin anaphylaxis may lead to sudden death. Hypersensitivity and infection by resistant organisms.

- P/C: Patients with history of allergy to other drugs. Monitor renal and haematological system when prolonged and high dose is given. Topical use with penicillin should be avoided because of the chances for sensitization.

- S/E: Penicillins are remarkably safe. The most important reactions to be feared is anaphylaxis. Jarisch Herxheimer reaction especially in syphilis. Miscellaneous reactions - nausea, vomiting, sterile inflammation at injection site. Accidental i.v. administration of procaine penicillin can cause anxiety, mental disturbances, paraesthesia, convulsions etc.

- P/A: Benzyl penicillin (Penicillin G)

Injection 5 lac, 10 lac units

Tablet 2 lac, 4 lac and 8 lac units.

Phenoxymethyl penicillin

Tablet 62.5 mg, 125 mg, 250 mg (250 mg = 4,00,000 units)

Procaine penicillin

Injection 3 lac, 15 lac and 30 lac units along with penicillin G

Benzathine penicillin

Injection 6 lac, 12 lac and 24 lac units.

- | | | |
|--------|-----------------------|-----------------------------------|
| Dose : | Penicillin G | 4 - 5 lac units, 6h. |
| | Penicillin V | 4 - 8 lac units, 6 h |
| | Procaine Penicillin | 6 - 12 lac units daily |
| | Benzathine penicillin | 12 - 24 lac units once in 3 weeks |

- A For mild infections such as streptococcal pharyngitis

i Penicillin V 250 - 500 mg, 6 h.

ii Benzyl penicillin 4,00,000 - 8,00,000 units orally, 6h

- B More severe infections such as uncomplicated pneumonia
Inj Benzyl penicillin 5,00,000 units in, 4-6 h.
- C For more severe infections such as empyema, meningitis
- Inj Benzyl penicillin 10 - 20 Lac units i.m., 4-6 h.
 - Inj Benzyl penicillin 20 Lac Units i.v., 2 h.
- D Prophylactic Use.
- Rheumatic Fever.
Inj Benzyl penicillin 5,00,000 units i.m. b.d. for 10 days.
Thereafter it should be continued with either intramuscular benzathine penicillin
1.2 million units every 3 weeks or oral penicillins.
 - Streptococcal infections
Oral benzyl penicillin in the dose of 2,00,000 units twice daily for 5 days or a single injection of 1.2 mega units of benzyl penicillin affords a satisfactory protection against *Streptococcus pyogenes*.
 - Recurrent lymphangitis
Benzathine penicillin 12,00,000 units once in a month can prevent recurrent lymphangitis and consequent lymphoedema.
- D/I: Antacids reduce absorption of orally administered ampicillin, probenecid reduces urinary excretion of penicillins. So it can be used therapeutically to increase blood levels of penicillin.
- Note : Whenever possible penicillin should be administered only after testing for hypersensitivity to avoid unexpected fatal reactions.*
- Cost : Benzyl penicillin Inj 10 lac units (vial) Rs. 7.00 - 8.00
Tab 4 lac units (90) Rs. 10.00 - 12.00
- Phenoxymethyl penicillin
Tab 250 mg (10) Rs. 7.00 - 17.00
- Procaine penicillin Inj 30 lac units +
20 lac unit penicillin G (vial) Rs. 28.00 - 30.00
- Benzathine penicillin Inj 24 lac units (vial) Rs. 21.00 - 25.00

A drop of weak solution containing 1000 unit / mL is tested on the forearm by a scratch test. If the test is negative 10000 units is given by intradermal test. If there is no reaction upto 30 min the drug may be given parenterally. In any case drugs for emergency resuscitation such as adrenaline, hydrocortisone and i.v. glucose, and respiratory support should be available at hand.

2.2.1.2 Beta lactamase resistant penicillins

Some of the betalactamase resistant penicillins have adequate absorption from GIT, e.g. cloxacillin, oxacillin, flucloxacillin, while the absorption of others is variable, e.g. methicillin, nafcillin, dicloxacillin. They have less potent antimicrobial activity against microorganisms that are sensitive to Penicillin G but they are effective against penicillinase producing *Staphylococcus*

aureus.

Cloxacillin ★

- I: Infections due to benzyl penicillin resistant staphylococci, mixed staphylococcal and streptococcal infection, prophylaxis of staphylococcal infection.

C/I:, P/C:, S/E:, D/I: Similar to that of Benzyl penicillin.

P/A: Capsules 250 mg, 500 mg

Injection 250 mg, 500 mg

Syrup 125 mg/5 mL

Combination preparations (tablet, injection, syrup) with ampicillin in different ratios are available.

Dose: Initial dose varies from 500 mg to 1 g, 6h. Maintenance dose 250 mg, 6h.

Can be given orally / i.m. or i.v.. If given orally it should be 1 h before / 2 h after meal.

Cost: Caps 500 mg (10) Rs. 40.00 - 55.00

Inj 250 mg (vial) Rs. 6.00 - 10.00

Syrup 125 mg/ 5 mL (24 g) Rs. 12.00 - 13.00

Methicillin

- I: Infection due to penicillinase producing staphylococci.

C/I:, P/C:, S/E:, D/I: Similar to that of benzyl penicillins.

P/A: Injection 1 g, 4 g, 6 g and 10 g.

Dose: 1g every 4 - 6 h, i.m. or i.v. infusion

Cost: Not freely available.

Nafcillin

- I: Infection due to staphylococci resistant to benzyl penicillin

C/I:, P/C:, S/E:, D/I: Similar to that of benzyl penicillins.

P/A: Tablet 500 mg

Capsules 250 mg

Injection 500 mg, 1 g, 2g, 10 g

Dose: 500 - 1 g 4 - 6 hrly

Cost: Not commercially available freely.

2.2.1.3 Broad spectrum penicillins

By modification of side chain of the betalactam ring of benzyl penicillin many useful derivatives with extended antimicrobial spectrum have been developed. They can be administered both orally and parenterally depending upon the severity of infection. Here the antimicrobial activity is extended to include such gram negative organisms like *H. Influenzae*, *E. coli*, *Proteus mirabilis*. Antibiotics under this group include ampicillin, amoxycillin.

becampicillin, pivampicillin, talampicillin. These antibiotics are also inactivated by betalactamases.

Ampicillin ✧

1. Ampicillin is used in infections due to gram positive cocci and bacilli, anaerobic organisms, neisseria, gram negative bacilli including *Bordetella pertussis*, *H. influenzae* and some enterobacteriaceae such as *E. coli*, *Proteus mirabilis*, gram negative cocci such as *Branhanella catarrhalis*, *N. meningitidis*.

It is used in urinary tract infection, respiratory tract infections, meningitis, bacterial endocarditis, biliary tract and intestinal infections, whooping cough, granuloma inguinale.

C/I, P/C, S/E, D/I: Similar to that of benzyl penicillin. Even though cross sensitisation may occur between the betalactum antibiotics the anaphylactic reactions are less dramatic compared to benzyl penicillin. Ampicillin should not be given to patients with infectious mononucleosis.

P/A:	Tablet	125 mg, 250 mg
	Capsules	250 mg, 500 mg
	Injection	100 mg, 250 mg, 500 mg and 1 g.
	Syrup	125 mg/5 mL, 250 mg/5 mL.
	Drops	100 mg/mL

Dose: Usual adult dose is 250 mg, 6h. In severe infections and if early results are required then 500 mg, 6h may be used.
 Meningitis 2 g, 4h; bacterial endocarditis 1-2 g, 3-4h, i.m. or i.v.
 Parenteral: 250 - 500 mg, 6 h, i.m. or slow i.v., injection or infusion.
 Children: 100 - 400 mg/kg/day in divided doses.

Cost:	Tab	125 mg	(10)	Rs. 14.00 - 18.00
	Caps	250 mg	(10)	Rs. 25.00 - 30.00
	Inj	500 mg	(vial)	Rs. 12.00 - 14.00
	Syrup	125 mg/5 mL	(30 mL)	Rs. 13.00 - 16.00
	Drops	100 mg/mL	(10 mL)	Rs. 8.00 - 22.00

The blood levels of ampicillin can be maintained at higher levels for the treatment of resistant and serious infection by administering probenecid. This is particularly useful for treatment of uncomplicated gonorrhoea. For the treatment of betalactamase producing organisms ampicillin can be administered along with a betalactamase inhibitor such as sulbactam. Alternatively penicillinase-resistant antibiotic such as cloxacillin or flucloxacillin should be used. In association with an aminoglycoside the antimicrobial spectrum can be increased.

Amoxycillin ✧

1. Similar to ampicillin

Blood levels are twice as high as those after a similar dose of ampicillin by oral route.

C/I:, P/C:, S/E:, D/I: Similar to that of benzyl penicillin.

P/A: Capsule 125 mg, 250 mg, 500 mg
 Tablet 125mg, 250 mg, 500 mg
 Injection 250 mg, 500 mg
 Syrup 125 mg/5 mL, 250 mg/5 mL
 Drops 100 mg/mL

Combination preparation with bromhexin, cloxacillin, carbocysteine and clavulanic acid are also available.

Dose: 250 - 500 mg 8h orally, can be given i.m/i.v.

For severe infections doses as high as 3 g, 12-24 h may be needed.

Cost:	Caps	500 mg (6)	Rs. 30.00 - 35.00
	Syrup	125 mg/5 mL (30 mL)	Rs. 12.00 - 25.00
	Inj	250 mg (vial)	Rs. 7.00 - 20.00
	Tab	250 mg (10)	Rs. 30.00 - 36.00
	Drops	100 mg/mL (10mL)	Rs. 14.00 - 18.00

Talampicillin

This is hydrolysed by tissue esterases in the intestinal wall and ampicillin is released into the circulation. Since it has no intrinsic antibacterial activity it is not likely to have direct effect on the bacterial flora of the gut.

I:, C/I:, P/C:, S/E:, D/I: Similar to that of bezyl penicillin.

P/A: Tablet 250 mg
 Syrup 125 mg/5 mL

Dose: 250 - 500 mg 3 - 4 times daily.

Cost: Not freely available.

2.2.1.4 Extended spectrum penicillins

Their spectrum includes pseudomonas, enterobacteriaceae and proteus. The drugs in this group are carbenicillin, ticarcillin and azlocillin. Others such as piperacillin and mezlocillin are active against klebsiella also.

Carbenicillin

I: Infection by Pseudomonas aeruginosa and proteus

C/I:, S/E:, D/I: Similar to that of benzyl penicillin.

P/C: Due to large sodium content it can produce cardiac failure in susceptible individuals. Platelet dysfunction and bleeding tendency may develop rarely.

P/A: Injection 1 g, 5 g

Dose: 2 g, 6h, i.m. Can be given slow i.v. infusion also.

Cost: Inj 1 g (vial) Rs. 22.00 - 25.00

Ticarcillin

I: Similar to that of carbenicillin.

C/I:, P/C:, S/E:, D/I: Same as for benzyl penicillin.

P/A: Injection 1g vial, 5 g infusion

Dose: 15 - 20 g / day

Give 5g diluted in 20 ml and injected i.v. over 3 - 5 min every 6 - 8h

Cost: Not freely available.

Piperacillin

I: Infection due to pseudomonas and klebsiella.

C/I, S/E: Similar to that of benzyl penicillin.

P/C: Dose modification according to creatinine clearance in case of renal impairment.

P/A: Injection 1g, 2g, 4g vials

Dose: Similar to ticarcillin.

D/I: Piperacillin may inactivate aminoglycosides.

Cost: Inj 2 g (vial) Rs. 149.00 - 215.00

Mezlocillin

I, C/I, S/E, P/C, D/I: Similar to that of piperacillin

Dose: 1.5 - 3 g, 6 h.

Cost: Not freely available.

2.2.2 CEPHALOSPORINS

They have 7 amino cephalosporanic acid nucleus which bears close resemblance to the 6 amino penicillanic acid nucleus of penicillins. Various cephalosporins, however differ in their antibacterial spectrum as well as in their resistance to betalactamase enzyme. They are bactericidal and act by inhibiting bacterial cell wall synthesis.

On the basis of spectrum of antimicrobial activity and period of introduction they are classified as shown below:

Classification of generation of cephalosporins

Generation	Salient feature	Example	Antimicrobial spectrum	Remarks
First	Good activity against gram +ve bacteria and relatively modest activity against gram -ve organism.	cefazolin cephalexin cephaloridine cefadroxil cefalothin	Streptococci except some penicillin resistant strains, staphylococci aureus except methicillin resistant organism. No activity against enterococci or listeria.	- Less painful, preoperatively for surgical procedures. - suprainfection with candida - prolonged activity duration

Second	Increased activity against gram -ve microorganisms. Activity against gram +ve cocci are less than that of first generation cephalosporins.	cefador cefuroxime cefoxitine cefotetan	E.coli, klebsiella proteus H.influenza, Moraxella catarrhalis, Bacteroides fragilis.	against mixed aerobic/ anaerobic organisms.
Third	Less activity than first generation against gram +ve cocci but more active against betalactamase producing strains of enterobacteriaceae and P. aeruginosa.	ceftizoxime cefixime cefoperazone ceftazidime cefotaxime ceftriaxone	enterobacteriaceae, serratia, N.gonorrhoeae added activity against P.aeruginosa added activity for S.aureus and S.pyogenes, Salmonella	good oral activity stable to hydrolysis
Fourth	Has extended spectrum of activity, increased stability from hydrolysis by plasmid- and chromosomally-mediated betalactamases.	cefepime	comparable to third generation. More activity against gram -ve organisms and staphylococci	

- I: Infections due to streptococci and the common gram negative pathogens such as *E.coli*, *klebsiella* and *proteus*, gram negative infections especially those caused by betalactamase producing organisms including *H.influenza*. They are active against *pseudomonas*, meningitis caused by gram negative bacteria, nosocomial infections, all forms of gonococcal infections, serious gram negative bacillary infections, pneumonia in cystic fibrosis, febrile leukopenia, infections of respiratory tract, urinary tract and skin, septicemia, mixed aerobic and anaerobic infections, otitis media.

C/I: Hypersensitivity, porphyria.

P/C: 1. i.v. injections can cause thrombophlebitis

2. i.m. injections are painful.

3. Large dose can cause renal damage. Nephrotoxicity is dose-related and is potentially reversible on drug withdrawal

4. Cross sensitivity with penicillin can occur in 10% of patients allergic to penicillin.

S/F: Skin rash, fever, serum sickness, anaphylactoid reactions, eosinophilia, neutropenia, transient splenomegaly, raised SGOT levels.

D/I: Colistin increase the incidence of renal toxicity. Ethanol with some cephalosporins result in disulfiram-like reactions possibly by producing acetaldehyde accumulations. Furosemide may enhance the nephrotoxicity of cephalosporins. Probenecid inhibits the renal excretion of cephalosporins.

2.2.2.1 First generation Cephalosporins**Cephazolin**

- P/A: Injection 125 mg, 250 mg, 500 mg and 1 g vial.
The constituted solution should be stored and protected from light and used within 24 h.
- Dose: 500 mg - 1 g i.m. or i.v., 6 - 8 h.
- Cost: Inj 250 mg (vial) Rs. 15.00 - 40.00

Cephalexin

- P/A: Tablet 125 mg, 250 mg, 500 mg
Capsule 250 mg, 500 mg.
Syrup 125 mg/5mL, 250 mg/5 mL.
Drops 100 mg/mL.
- Dose: 250 mg - 1 g, 6 - 8 h., oral
- Cost: Cap 500 mg (10) Rs. 70.00 - 120.00
Tab 250 mg (10) Rs. 40.00 - 60.00
Syrup 125 mg/5 mL (40 mL) Rs. 20.00 - 25.00
Drops 100 mg/mL (10 mL) Rs. 27.00 - 30.00

Cephaloridine

- P/A: Injection 500 mg, 1g, vial
- Dose: 500 mg i.m. or i.v., 6 - 8 h
- Cost: Inj 500 mg (vial) Rs. 30.00 - 90.00

Cefadroxil

- P/A: Tablet 125 mg, 250 mg, 500 mg, 1g.
Capsules 500 mg
Syrup 125 mg/5 mL, 250 mg/5 mL
Drops 100 mg/mL
- Dose: 500 mg - 1 g, 6 - 8 h., oral
- Cost: Tab 500 mg (4) Rs. 50.00 - 55.00
Cap 500 mg (4) Rs. 42.00 - 55.00
Syrup 125 mg/5mL (40 mL) Rs. 20.00 - 25.00
Drops 100 mg/mL (10 mL) Rs. 35.00 - 38.00

Cephalothin

- P/A: Injection 1g, 2g.
- Dose: 500 mg - 2 g i.m. or i.v., 4 - 6 h.
- Cost: Inj Not freely available

2.2.2.2 Second generation cephalosporins**Cefaclor**

- P/A: Tablet 375 mg
Capsule 250 mg
Syrup 125 mg/5mL, 187 mg/5 mL
Drops 50 mg/mL
- Dose: 250 - 500 mg, 6 - 8 h., oral

Cost :	Cap	250 mg	(10)	Rs. 165.00 - 170.00
	Tab	375 mg	(6)	Rs. 160.00 - 165.00
	Syrup	125 mg/5mL	(30 mL)	Rs. 50.00 - 75.00
	Drops	50 mg/mL	(10 mL)	Rs. 35.00 - 40.00

Cefuroxime

P/A :	Tablet	125 mg, 250 mg, 500 mg		
	Capsules	250 mg		
	Injection	250 mg, 750 mg, 1.5 g		
Dose :	250 - 500 mg, 12 h, oral; 750 mg - 1.5 g i.m. or i.v., 8 h.			
Cost :	Inj	250 mg	(vial)	Rs. 45.00 - 70.00
	Tab	250 mg	(4)	Rs. 140.00 - 160.00
	Cap	250 mg	(4)	Rs. 130.00 - 140.00

Cefoxitin

P/A :	Injection	1g, 2g
Dose :	1 - 2 g i.m. or i.v., 8 h.	
Cost :	Not freely available	

Cefotetan

P/A :	Injection	1 g, 2 g, 10 g
Dose :	1 - 2 g i.v. or i.m., 12 h.	
Cost :	Not freely available	

2.2.2.3 Third generation cephalosporins

Ceftizoxime

P/A :	Injection	500 mg, 1 g
Dose :	1 - 2 g i.m. or i.v., 8 - 12 h.	
Cost :	Inj 500 mg	(vial) Rs. 120.00 - 125.00

Cefixime

P/A :	Tablet	200 mg, 400 mg
	Capsules	100 mg
Dose :	200-400 mg/day in 1-2 divided doses, oral	
Cost :	Cap 100 mg	(4) Rs. 200.00 - 205.00
	Tab 200 mg	(4) Rs. 330.00 - 340.00

Cefoperazone

P/A :	Injection	500 mg, 1 g, 2 g.
Dose :	Cefoperazone 1 - 2 g i.m. or i.v., 8 - 12 h.	
Cost :	Inj 2 g	(1 vial) Rs. 400.00 - 420.00

Ceftazidime

P/A :	Injection	250 mg, 500 mg, 1 g.
Dose :	1 - 2 g i.m. or i.v., 8 - 12 h.	
Cost :	Inj 250 mg	(vial) Rs. 90.00 - 115.00

Cefotaxime

P/A: Injection 125 mg, 250 mg, 500 mg, 1 g, 2 g
 Dose: 1 - 2 g i.m. or i.v., 8 h.
 Cost: Inj 250 mg (vial) Rs. 20.00 - 25.00

Ceftriaxone

P/A: Injection 125 mg, 250 mg, 500 mg, 1 g.
 Dose: 1 - 2 g i.m. or i.v., 12 - 24 h.
 Cost: Inj 250 mg (vial) Rs. 45.00 - 55.00

2.2.2.4 Fourth generation cephalosporins

Cefepime

Dose: 2 g i.v., 12 h.
 Cost: Not freely available.

2.2.3 AMINOGLYCOSIDES

The aminoglycoside antibiotics include streptomycin, gentamicin, kanamycin, tobramycin, amikacin, netilmicin, neomycin, framycetin, paromomycin. These are polycations containing aminosugars in glycoside linkage. They are bactericidal. Bacteria develop resistance to them fairly rapidly and may even exhibit cross resistance among different aminoglycosides. They exhibit synergism when combined with a betalactam antibiotic such as penicillin or cephalosporin. They are not adequately absorbed when given orally, their distribution is essentially extra cellular. Diffusion into C.S.F (except in the neonate) and into the eye is poor after systemic administration. High concentrations are found in the renal cortex and in the endolymph and the perilymph of the inner ear and therefore these organs are particularly liable to suffer from toxic effects. Excretion is through kidneys.

Streptomycin ✧

- I: Tuberculosis, bacterial endocarditis, tularemia, plague, brucellosis
- C/I: Hypersensitivity, neonates, pregnancy, lactation
- P/C: Renal or hepatic insufficiency, concurrent use with other ototoxic and nephrotoxic drugs. Elderly develop giddiness and vestibular disturbances, hence dose may have to be reduced. Use with caution in infants.
- S/E: Local irritation, intolerance, ototoxicity (damages the vestibular part of the 8th cranial nerve), mild albuminuria, rarely optic neuritis and peripheral neuritis.
- P/A: Injection 0.75 g and 1 g
- Dose: Adult 1 - 2 g/day (15 to 25 mg/kg/day) i.m.; 100 mg/day intrathecal.

Children : 20-40 mg/kg/day i.m. ; 10 mg/day intrathecal.

Tuberculosis : 0.75 g/day

Bacterial endocarditis : 0.5 g b.d. with penicillin

Tularemia : 1 - 2 g/day 7 - 10 days.

Plague : 1 - 4 g/day 7 - 10 days.

Brucellosis: 1 g/day for 1st 3 weeks with tetracycline.

D/I: Tetracycline and chloramphenicol may reduce the therapeutic efficiency of streptomycin. Nephrotoxicity is increased by combination with capreomycin, amphoterecin-B, ethacrynic acid and cyclosporin.

Cost : Inj 1 g (vial) Rs. 9.00 - 10.00

Gentamicin ☆

I: Urinary tract infection. Pneumonia caused by pseudomonas aeruginosa, klebsiella, E.coli or proteus and mycoplasma, Meningitis - specially pseudomonas and acinetobacter (which are resistant to betalactams); Peritonitis, enterococcal endocarditis, gram-negative bacillary species, group A β haemolytic streptococci, and staphylococci.

C/I : Pregnancy, lactation and known sensitivity to the drug.

P/C: Chronic renal failure, myasthenia gravis, hearing disorders, reduced dose in elderly and children.

S/E: Nephrotoxicity, irreversible ototoxicity.

P/A: Injection 10, 20, 40, 60 and 80 mg/mL

Drops 0.3% w/v

Ointment (in combination with steroids)

Dose: i.m. or i.v. 2 - 5 mg/kg/day in 3 divided doses in persons with normal renal function. It should be reduced in renal damage.

Intrathecal dose 1 - 5 mg/day.

D/I: Same as streptomycin. Concurrent use of antiemetics mask ototoxicity.

Note : *Topical application should be avoided as far as possible since they may produce bacterial resistance.*

Cost: Inj 40 mg/mL (2 mL) Rs. 7.00 - 8.00

Drops 0.3 % w/v (5 mL) Rs. 5.00 - 8.00

Kanamycin

I: Kanamycin is effective against UTL, septicemia, meningitis, bacterial endocarditis, GIT infection and pelvic infections by gram -ve and gram +ve organisms. It has mild anti T.B activity and is used as second line anti T.B drug

C/I: Similar to gentamicin but milder.

P/C: Use with caution in Parkinsonism, myasthenia gravis and renal impairment.

S/E, D/I : Same as other aminoglycosides.

P/A: Capsules 500 mg.
Injection 500 mg , 750mg and 1g

Dose : 15 mg/kg/day (2 or 4 divided doses)

Oral preparation mainly used to sterilize intestine preoperatively and in the treatment of hepatic coma. It is seldom used now for this purpose.

Cost : Inj 500 mg (vial) Rs. 15.00 - 16.00
Capsules are not freely available.

Tobramycin

I: Tobramycin is superior against pseudomonas. Therefore bacteremia, osteomyelitis and pneumonia caused by pseudomonas respond better to combination of tobramycin with penicillins or ceftazidime.

C/I, P/C : Similar to that of aminoglycosides.

S/E: Nephrotoxicity and ototoxicity, but less compared to gentamicin.

P/A: Injection 10 mg, 20 mg, 40 mg, 60 mg and 80 mg
Eye drops 0.3 % w/v
Eye ointment : 0.3% w/w.

Dose : 3 mg/kg/day in 3 divided doses.

D/I: Same as streptomycin.

Cost : Inj 20 mg (2 mL) Rs. 12.00 - 13.00
Other preparations are not freely available.

Amikacin ☆

I: Most strains of serratia, proteus, pseudomonas, klebsiella, enterobacteria, and E.Coli. are sensitive.

Used in atypical mycobacterial infections and serious nosocomial gram negative infection

C/I: Hypersensitivity, pregnancy, lactation.

P/C: Same as gentamicin

S/E: Cochlear damage, nephrotoxicity.

P/A: Injection 50 mg, 100mg, 250mg, 500mg.

Dose : Amikacin sulphate 15 mg/kg/day 2 or 3 divided doses. i.m. and i.v.

D/I: Ethacrynic acid increases nephrotoxicity and ototoxicity. Neuromuscular blocking drugs increases neuromuscular blocking action of aminoglycosides. Penicillins, cephalosporins and newer beta lactam antibiotics act synergistically with amikacin.

Cost : Inj 100 mg (vial) Rs. 16.00 - 17.00

Netilmicin

I: Urinary tract infections, serious systemic infections, enterobacteriaceae and gentamicin resistant pathogens.

- C/I: Hypersensitivity.
 P/C: Neurotoxicity and nephrotoxicity - use with caution.
 S/E: Same as other aminoglycosides, but milder.
 P/A: Injection 10, 25, 50 and 100 mg/mL.
 Dose : Urinary tract infections 1.5 - 2 mg/kg/day in 2 divided doses.
 Serious systemic infections 4 - 6.5 mg/kg/day as (2 or 3 doses)
 Children - 5.5 - 8 mg/kg/day (2 - 3 doses)
 Neonates - 4 - 6.5 mg/kg/day (2 doses)
 D/I: Same as aminoglycosides.
 Cost : Inj 50 mg (1mL) Rs. 67.00 - 68.00

Neomycin ☆

- I: Topical application for burns, ulcers, dermatosis.
 Infections by enterococci, streptococci, staphylococci, B.anthraxis, C.diphtheriae, H.influenza, H.pertusis, proteus, pasteurilla, salmonella, shigella.
 Preparation of the bowel for surgery.
 Adjunct for hepatic coma.
 C/I: Hypersensitivity and renal impairment.
 P/C: Malabsorption syndrome on chronic use.
 S/E: Hypersensitivity reactions, rashes, nephrotoxicity and ototoxicity, malabsorption and super infection.
 P/A: Tablets 500 mg
 Capsules 350 mg
 Suspension 125 mg/5 mL
 Ointments/creams 5 mg/g.
 Dose : 0.25 - 1 g q.d.s. as oral capsules for sterilizing bowel.
 D/I: Same as streptomycin.
 Note : *Neomycin has been combined with different steroids and polymixin B and bacitracin for topical application.*
 Cost : Cap 350 mg (10) Rs. 26.00 - 30.00
 Other preparations are not freely available.

Framycetin ☆

- I: Staphylococcal skin infections and nasal carriers of staphylococci.
 Clinically used for otitis externa, ocular infections like conjunctivitis, blepharitis and keratitis.
 Primary and secondary skin infections and burns.
 C/I: Hypersensitivity, perforated ear drum, resistant infection
 P/C: Increased risk of toxicity on application to large area, caution when used in elderly and children, and those with renal failure
 S/E: Sensitisation, contact dermatitis, irritation and itching
 P/A: Drops 0.5%
 Ointment 0.5%

2. Anti Infective Agents

Dressings 1%

Dose : Used as 0.5 % ointment for staphylococcal skin infections & nasal carriers of staphylococci.

D/I: Same as streptomycin.

Cost : Drops 0.5 % (5 mL) Rs. 6.00 - 7.00
Ointment 0.5% (5g) Rs. 6.00 - 8.00
Dressings 1% (10 x 10 cm) Rs. 14.00 - 15.00

Paromomycin

I: Chronic bacillary dysentery, sterilization of bowel for surgery, hepatic coma. It has considerable activity against *E. histolytic*.

C/I: Hypersensitivity, intestinal obstruction.

P/C: Consult physician if hearing impairment or dizziness occur. Super infection may occur.

S/E: Headache, emesis, diarrhoea and skin rashes.

P/A: Capsule, Syrup.

Dose: Hepatic coma : 4 g followed by 2 g/day in 4 divided doses.

Intestinal amoebiasis : 25 - 35 mg/kg/day in 3 divided doses with meals for 5 - 10 days.

D/I: Same as streptomycin.

Cost : Not freely available in India.

2.2.4 TETRACYCLINES ☆

They are bacteriostatic antibiotics which have wide range of antimicrobial activity against gram positive and gram negative bacteria. They interfere with protein synthesis of the microbial organism.

I: They are the drugs of choice for rickettsia, mycoplasma and ureaplasma. They are also effective in coccal infections, chronic respiratory infections by *H. influenzae*, *klebsiella*, other infections by *E. coli*, *brucella*, and plague. Due to their higher toxic effects and only bacteriostatic activity, their use is limited to specific infections where others safer bactericidal antibiotics are not effective.

C/I: Impaired renal/ hepatic function and hypersensitivity, children less than 8 years, SLE, blood dyscrasias, pregnancy, lactation.

P/C: Use with caution in elderly and patients with benign intracranial hypertension. Superinfection with proteus, candida albicans, pseudomonas or clostridium may occur. In long term therapy hepatic, renal and haemopoietic function should be monitored. Supplementation of B complex factors is necessary since long term therapy suppresses the intestinal bacteria.

S/E: Intolerance eg. rashes, photosensitivity, nail discoloration etc., G.I disturbances- nausea, vomiting, diarrhoea, superinfection, hepatic

failure, pancreatitis, renal impairment, weight loss. Tetracycline orthophosphate deposits on developing teeth and bones. Benign intracranial hypertension. i.v. tetracyclins cause phlebotrombosis.

P/A: Tablets 250 mg, 333 mg and 500 mg.

Capsule 250 mg, 333 mg and 500 mg.

Injection 100 mg, 250 mg and 500 mg

Topical Ointment 3 %

Topical Solution 2.2 mg/mL after reconstitution.

Dose: Oral : 250 - 500 mg, 6 h.

Parenteral : 300 mg 8 h i.m, 250 - 500 mg, 12 h i.v.

Take on an empty stomach 1 h before or 2 h after food with one glassful of water.

D/I: Antacids, calcium supplements, iron supplements, magnesium containing laxatives, antihypertensives like ACE inhibitors, diary products, oral iron and ulcer healing drugs like sucralfate reduces absorption. Contraceptives increases incidence of breakthrough bleeding. Concurrent use with Vit. A cause benign intracranial hypertension. Increased blood levels with carbamazepine and phenytoin.

Several analogues and derivatives of tetracycline have been developed. They include doxycycline, demeclocycline, methacycline, minocycline, chlortetracycline and oxytetracycline. However only a few are in general use.

Cost: Caps 250 mg (10) Rs. 12.00 - 13.00

Tab 250 mg (10) Rs. 13.00 - 14.00

Other preparations are not freely available.

Chlortetracycline

I: Ocular infection by *S.aureus*, *Strep.epidemicus*, *S.pneumoniae*, *H.influenzae* etc, trachoma, chlamydia infection, keratitis.

C/I: Hypersensitivity.

P/C, S/E, D/I : Same as tetracycline.

P/A: Ophthalmic ointment 1 %.

Topical ointment 3%.

Dose: For local application 2 - 3 times daily.

Cost : Not freely available in India.

Oxytetracycline

I: External bacterial infection of the eye, mixed bacterial infection of respiratory, GI and GU system, psittacosis.

C/I: Hypersensitivity, below 8 years of age, SLE, neonates, pregnancy, lactation.

P/C: Elderly, hepatic or renal damage.

2. Anti Infective Agents

- S/E: Same as tetracycline. Rarely fulminant diarrhoea in post operative patients.
- P/A: Capsules 250 mg, 500 mg
Injection 50 mg/mL
Ophthalmic ointment 10 mg/g
Topical ointment 30 mg/g
- Dose: Oral: 1-2 g daily in 4 divided doses.
Parenteral: 250 - 500 mg/day in divided doses 8 h i.m.
- D/I: Potentiates methoxyflurane nephrotoxicity, interferes with anticoagulant control, cause failure of oral contraception, interferes with bactericidal effect of penicillins.
- Cost: Caps 250 mg (8) Rs. 7.00 - 8.00
Inj 50 mg/mL (10 mL) Rs. 7.00 - 8.00
Oph. oint. 10 mg/g (3 g) Rs. 3.00 - 4.00
Topical oint. 30 mg/g (30 mg/g) Rs. 15.00 - 16.00

Doxycycline ✧

Doxycycline is a semi synthetic tetracycline

- P/A: Tablet 50 mg, 100 mg, 200 mg
Capsule 100 mg
Syrup 25 mg/5 mL, 50 mg/5 mL.
- Dose: 200 mg (single dose) on day one followed by 100 mg o.d. Severe infections 100 mg b.d. for 5-10 days.
Children 3 - 4 mg/kg/day in divided doses.
- Cost: Tab 100 mg (10) Rs. 29.00 - 30.00
Caps 100 mg (10) Rs. 16.00 - 23.00
Syrup 25 mg/5mL (30 mL) Rs. 14.00 - 15.00

2.2.5 MACROLIDES

Macrolides derive their name due to the presence of many numbered lactone ring to which are attached one or more deoxy sugars, e.g., erythromycin, clarithromycin, azithromycin, oleandomycin, roxithromycin and spiramycin. They were all originally derived from fungi.

Their antimicrobial spectrum include *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, gonococci, mycoplasma, *H. influenzae*, legionella, brachyella.

Erythromycin

- I: Acute bacterial pharyngitis, tonsillitis, sinusitis, otitis, mastitis, cellulitis, mycoplasma pneumonia, diphtheria, pertussis, endemic trachoma, legionellosis, *Campylobacter jejuni* enteritis, bacillary angiomatosis, acne, leptospirosis, Lyme disease, endocarditis, prophylaxis before dental procedure, community acquired pneumonia, relapsing fever, tetanus in patients allergic to penicillin, nocardiosis.

- C/I: Hypersensitivity to erythromycin, history of jaundice.
P/C: Cholestatic hepatitis and history of hepatic disease, pregnancy, lactation.
S/E: Mild GI upset - nausea, diarrhoea, abdominal pain, rash, hepatitis.
P/A: Available as erythromycin estolate and erythromycin stearate.

Tablet 100, 125, 250, 333, 400, 500 mg.

Capsules 250 mg

Suspension 100 mg/5 mL, 125 mg/5 mL, 250 mg/5 mL.

Lotion 2 %, 3%w/v

Drops 100 mg/mL

Creams 3%w/w

Ointment 2% w/w, 3% w/w

Gel 4% w/w

Dose: Mycoplasma pneumonia : 250 - 500 mg, 6h for 14 - 21 days.

Respiratory diphtheria : 500 mg, 6h i.v. for 14 days

Cutaneous diphtheria : 500 mg, 6h for 7 days.

Pertussis : 50 mg/kg maximum of 2 g/day in 2 - 4 divided doses for 14 days.

Endemic trachoma : ointment locally for 21- 60 days. Mass application for affected community.

Inclusion conjunctivitis : Treatment for 3 weeks.

Legionellosis : 500 mg - 1g oral, 6 h for 10 - 14 days.

Campylobacter jejuni enteritis : 250 mg, 6h for 5 - 7 days.

Bacillary angiomatosis : 500 mg oral o.d. for 2 months in immunocompromised.

Acne : 250 mg-1 g o.d., oral for 5 days.

Lyme disease : as a 4th choice alternative; localized lesions - 250 mg 6h for 10 days, disseminated lesions - 250mg, 6 h for 20 - 30 days.

Endocarditis, prophylaxis before dental procedure; 800 mg-1 g, 2 h before procedure followed by half the dose 6 hours later, orally.

Community acquired pneumonia (typical) : 500 mg, 6h for 7 - 10 days

Louse borne relapsing fever : 500 mg single dose

Tick borne relapsing fever: 500 mg, 6h for 7 days.

Acute bacterial pharyngitis, tonsillitis, sinusitis, otitis, mastitis, cellulitis, tetanus in patients allergic to penicillin : 250 mg, 6 h for 7 - 10 days.

Nocardiosis: 500 - 750 mg q.d.s. for 6 weeks - 1 year

- D/I: Increases absorption of alcohol; increased risk of cardiotoxicity with astemizole and terfenadine; increased plasma concentration and toxicity of carbamazepine or valproic acid, antagonises effect of chloramphenicol and lincomycin, increased risk of nephrotoxicity with cyclosporins, increases plasma digoxin levels by increasing the

2. Anti Infective Agents

absorption from the gut; enhances vasospasm associated with ergotamine, increases risk of rhabdomyolysis with lovastatin, increases pharmacological effect of midazolam and triazolam by decreasing the plasma clearance, increased potential for ototoxicity with other ototoxic medications in patients with renal impairment; interferes with bactericidal action of penicillins, increases serum xanthine concentration and toxicity; increases risk of haemorrhage especially in the elderly receiving long term warfarin therapy.

Cost:	Tab	250 mg	(10)	Rs. 33.00 - 35.00
	Caps	250 mg	(10)	Rs. 40.00 - 42.00
	Susp	125 mg/5mL	(60 mL)	Rs. 21.00 - 33.00
	Lotion	2% w/v	(20 mL)	Rs. 25.00 - 27.00
	Drops	100 mg/mL	(10 mL)	Rs. 24.00 - 25.00
	Cream	3% w/w	(20 g)	Rs. 29.00 - 42.00
	Oint	3% w/w	(10 g)	Rs. 15.00 - 16.00
	Gel	4 % w/w	(20 g)	Rs. 37.00 - 41.00

Clarithromycin

- I: *Mycoplasma pneumoniae*, *mycobacterium leprae*, community acquired 'typical pneumonia', atypical mycobacterial infection, prophylaxis against MAC, *H.pylori*, nocardiosis, upper and lower respiratory tract infections, skin and soft tissue infections.
- C/I: Patients hypersensitive to macrolides. Patients on terfenadine or astemizole, cardiac abnormality or electrolyte disturbance, safety in pregnancy and lactating period is not established.
- P/C: Caution should be exercised in patients with impaired hepatic function or with moderate to severe renal impairment, not recommended in children.
- S/E: Headache, skin rashes and transient elevation of liver enzymes, hepatic dysfunction with or without jaundice, psychosis, pseudomembranous colitis, Stevens Johnson syndrome, anaphylaxis.
- P/A: Tablet 250 mg, 500mg.
- Dose: *Mycoplasma pneumoniae* : 500 mg b.d. for 14 - 21 days.
Community acquired 'typical pneumonia' : 500 mg b.d for 7 - 10 days.
Atypical mycobacterial infection : 500 mg b.d till culture negative, or for 12 months
Prophylaxis against MAC : 500 mg o.d. / b.d.
Eradication of *H.pylori* : Dual therapy - 500 mg t.d.s. for 2 weeks with omeprazole.
New triple therapy - 250 mg b.d. for 1 week with omeprazole and metronidazole or 500 mg b.d. with omeprazole and amoxycillin for 1 week.
Nocardiosis : 500 mg b.d. for 6 months - 1 year.
- D/I: Same as for erythromycin. Rifampicin decreases serum concentration of clarithromycin, zidovudine delays the action.
- Cost: Tab 250 mg (4) Rs. 110.00 - 140.00

Azithromycin

- I: Genital chlamydial infection, mycoplasma pneumonia, community acquired typical pneumonia, non-tuberculosis mycobacteria, prophylaxis against mycobacterium avium complex (MAC).
- C/I: Hypersensitivity
- P/C: Impaired liver or renal function, pregnancy, lactation and children.
- S/E: Nausea, vomiting.
- P/A: Tablet 100 mg
Capsules 250 mg
Syrup/Susp 200 mg/5 mL
- Dose: 250 mg, 1 h before or 2 h after meal.
- Genital chlamydial infection : 1g single dose; treatment of sex partner also.
- Mycoplasma pneumonia : 500 mg on day 1 followed by 250 mg o.d. for 14 - 21 days.
- Community acquired typical pneumonia : 500 mg o.d. on day 1 followed by 250 mg o.d. for 4 days.
- Non-tuberculosis mycobacteria : 250 - 500 mg/day till culture negative for 12 months.
- Prophylaxis against MAC 1200 mg/week.
- D/I: Antacids decrease the peak serum concentration of azithromycin.
- | | | | |
|-------|------------|---------------------|---------------------|
| Cost: | Tab | 100 mg(3) | Rs. 40.00 - 41.00 |
| | Caps | 250 mg(6) | Rs. 132.00 - 590.00 |
| | Syrup/Susp | 200 mg/5mL (7.5 mL) | Rs. 45.00 - 48.00 |

Oleandomycin

- I: Pneumococcal pneumonia, group A b-haemolytic streptococcal infections of the upper respiratory tract.
- C/I: Hypersensitivity, pregnancy, lactation.
- P/C: Use with caution in patients with impaired hepatic function. Prolonged or repeated therapy may result in superinfection with nonsusceptible organisms leading to secondary infections.
- S/E: Anaphylaxis, urticaria, skin rashes, abdominal cramps, nausea, vomiting, diarrhoea.
- P/A: Capsules 250 mg
- Dose: Adult 250 - 500 mg q.d.s.
Children 125 - 250 mg, 6 h.
- D/I: Increased risk of intrahepatic cholestasis due to decreased metabolism of contraceptives on concurrent use with oleandomycin. Increased theophylline toxicity, increases CNS depression of triazolam.
- Cost: Not freely available.

Roxithromycin

- I: Antimicrobial spectrum is same as that of erythromycin. Higher concentration achieved in pulmonary, prostate and tonsillar tissue and in tear and pleural fluids. Useful in pneumonia, acute bronchitis, sinusitis, pharyngitis, tonsillitis, genital infection.
- C/I: Concomitant use of ergotamine type compounds
- P/C: Hepatic dysfunction.
- S/E: Nausea, vomiting, diarrhoea, skin rash, transient rise in liver transaminases.
- P/A: Tablet 50 mg, 150 mg, 300 mg
Liquid 50 mg/5 mL.
- Dose: 150 mg b.d. or 300 mg o.d., oral for 10 - 14 days.
- D/I: Increases the absorption of digoxin; increases half life of midazolam; displaces disopyramide from its protein binding sites; increases serum level of terfenadine leading to ventricular arrhythmias.
- Cost: Tab 150 mg (10) Rs. 70.00 - 130.00
Liquid 50 mg/5 mL (30 mL) Rs. 35.00 - 40.00

Spiramycin

- I: Respiratory infections, prostatitis, urethritis, skin infections, toxoplasmosis during pregnancy.
- C/I: Meningitis, hypersensitivity
- P/C: Same as for erythromycin.
- S/E: Nausea, vomiting, abdominal pain, urticaria, benign hepatitis.
- P/A: Tablet 1.5 million iu, 3 million iu
Suspension 0.37 million iu/5 mL
- Dose: Toxoplasmosis in pregnancy - 6 - 9 million iu (4 - 6 tab) in 2- 4 divided dose for 3 weeks. Repeated at 2 weekly intervals till delivery.
- D/I: Food reduces bioavailability. It increases blood level of theophylline and carbamazepine, warfarin and digoxin.
- Cost: Tab 1.5 million iu (10) Rs. 47.00 - 51.00
Susp 0.37 million iu/5mL (60 mL) Rs. 30.00 - 40.00

2.2.6 CHLORAMPHENICOL

- I: Effective against gram +ve and gram -ve organisms, rickettsias, chlamydias and mycoplasmas. Clinical indications include enteric fever, meningitis, H.influenzae, cystic fibrosis and infections resistant to other antibiotics.
- C/I: Hypersensitivity, minor infections, blood dyscrasias, bone marrow depression, pregnancy, lactation and porphyria.
- P/C: Use with caution in renal or hepatic diseases. Blood examinations to be done periodically.

S/E: Bone marrow depression, Grey syndrome, irreversible aplastic anaemia, peripheral neuritis, optic neuritis, nocturnal haemoglobinuria, tingling, impaired vision, weakness.

P/A: Tablet 250 mg
Capsules 125 mg, 250 mg, 500 mg
Syrup 125 mg/5 mL
Injection 500 mg, 1 g
Aplicaps 1 %
Eye Drops 0.4, 0.5, 1 %
Ointment 1 %
Ear Drops 5 %

Dose: Adults: 50 mg/kg/day oral, i.m., i.v. in 4 divided doses
Children - neonates : 25 mg/kg/day
2-4 week: 50 mg/kg/day
> 4 week : 75 mg/kg/day
Ear infection : 2 to 3 drops b.d. - t.d.s.
Eye infection : use drops or ointment b.d. - q.d.s.

D/I: Increases the effect of phenytoin, oral antidiabetics, oral anticoagulants. Phenobarbitone and rifampicin may reduce the effect of chloramphenicol. Chloramphenicol may inhibit the antibacterial effect of penicillins. Paracetamol may prolong the duration of action of chloramphenicol.

Cost:	Tablet	250 mg	(10)	Rs. 8.00 - 10.00
	Capsules	250 mg	(10)	Rs. 18.00-24.00
	Syrup	125 mg/5 mL	(60 mL)	Rs. 14.00 - 32.00
	Injection	1 g	(vial)	Rs. 12.00 - 34.00
	Aplicaps	1 %	(50 Nos.)	Rs. 22.00 - 25.00
	Eye Drops	1 %	(5 mL)	Rs. 5.00 - 7.00
	Ointment	1 %	(3 g)	Rs. 5.00 - 6.00
	Ear Drops	5 %	(5 mL)	Rs. 8.00 - 10.00

2.2.7 POLYENE ANTIBIOTICS

The commonly used drugs in this groups are bacitracin, polymyxin-B and colistin.

Bacitracin

It is a polypeptide antibiotic consisting of a group of polypeptides predominantly bacitracin A.

I: Its antimicrobial spectrum is similar to that of penicillins - mainly gram positive organisms. It is also effective against meningococci and gonococci, treponema, H-influenzae.

C/I: Hypersensitivity

P/C: Parenteral use (i m) causes nephrotoxicity, absorption from open wound, bladder or peritoneal cavity may lead to adverse reactions, avoid concurrent use with nephrotoxic drugs, restrict use in infants, monitor renal function frequently.

S/I: Nephrotoxicity, allergic disorders, albuminuria, azotemia

2. Anti Infective Agents

- P/A:** Injection 50,000 units vial
Eye ointment(combination with polymixin and neomycin) 500 units/g.
Powder (combination with polymixin and neomycin) 400 units/g
- Dose:** 1,000 units/kg/ day in 2-3 divided doses.
- D/I:** Increases risk of respiratory paralysis and renal dysfunction with aminoglycosides, neuromuscular blockade may be enhanced with nondepolarizing muscle relaxants.
- Cost:** Injection - not freely available.
Eye ointment(combination with polymixin and neomycin) 500 units/g (5 g) Rs. 15.00
Powder (combination with polymixin and neomycin) 400 units/g. (10 g) Rs. 16.00 - 17.00

Polymyxin - B

- I:** Polypeptide antibiotic effective against gram negative organisms particularly *Pseudomonas aeruginosa*.
Used in systemic infection, urinary tract infection, topical application in skin and eye infection
- C/I:** Hypersensitivity, pregnancy, lactation.
- P/C:** Renal dysfunction, myasthenia gravis, perforated tympanic membrane. Monitor renal functions.
- S/E:** Pain at site of injection, flushing, parasthesias, nephrotoxicity, ototoxicity.
- P/A:** Injection 5,00,000 iu (vial)
Eye drops 5,000 iu/mL
Ointment 5,000 iu
- Dose:** 15,000 iu - 25,000 iu/kg/ day for 7 - 10 days
- D/I:** Muscle relaxants - enhanced muscle relaxant effect, increased nephrotoxicity with cephalosporins and aminoglycosides. Synergistic effect with rifampicin.
- Cost:** Inj 5,00,000 iu (vial) Rs. 269.00 - 270.00
Oint 5,000 iu (3 g) Rs. 8.00 - 9.00
Eye drops 5,000 iu/mL (5 mL) Rs. 12.00 - 13.00

Colistin

- I:** It is a polypeptide antibiotic with similar spectrum to that of polymyxin B but slightly less active.
- C/I:** Hypersensitivity, myasthenia gravis, pregnancy, lactation.
- P/C:** Impaired renal function, porphyria, perforated tympanic membrane.
- S/E:** Circumoral or lingual paresthesia, nausea, skin rash, nephrotoxicity, ototoxicity, leukopenia, granulocytopenia, hepatotoxicity, superinfection with proteus, neurological disturbances.

- P/A: Syrup 12.5 mg/5 mL (2,50,000 iu)
 Dose: 3 - 5 mg/kg/day in divided doses
 D/I: Increases effect of muscle relaxants, increased nephrotoxicity with aminoglycosides.
 Cost: Syrup 250000 iu (30 mL) Rs. 17.00 - 20.00

2.2.8 QUINOLONES

Fluroquinolones are a group of synthetic bactericidal agents structurally related to nalidixic acid. They are very effective against gram negative bacilli and cocci including Enterobacteriaceae, H.influenzae and N.gonorrhoea. They are also active against P.aeruginosa, but less active against gram positive cocci and anaerobic bacteria. They are effective orally and parenterally. Commonly used drugs in this group are norfloxacin, ciprofloxacin, pefloxacin, ofloxacin, lomefloxacin and sparfloxacin.

Norfloxacin ☆

- I: Effective against gram negative organisms, urinary tract infection, STD, GI infection, prophylactic against sepsis, eye infections including conjunctivitis, keratitis and corneal ulcer.
 C/I: Pregnancy, lactation and children < 3 years.
 P/C: Use with caution in patients with renal impairment, history of epilepsy, dehydration. Monitor urinary output.
 S/E: Nausea, epigastric distress, abdominal cramps, rash, anorexia, diarrhoea.
 P/A: Tablet 100 mg, 200 mg, 400 mg, 800 mg
 Eye Drops 0.3% w/v 5 mL
 Eye oint. 0.3% w/w 5 g
 Combination preparation with tinidazole is also available.
 Dose: 400 mg b.d. for 7 - 14 days.
 D/I: Antacids reduce absorption, anticoagulant effect of nicoumalone and warfarin enhanced, increased risk of nephrotoxicity with cyclosporin, absorption reduced by oral iron, increases plasma theophylline concentration, sucralfate reduces the absorption, probenecid reduces excretion (increased side effects), reduces absorption of zinc.
 Cost: Tab 400 mg (10) Rs.20.00 - 60.00
 Eye Drops 0.3% w/v (5 mL) Rs.8.00 - 11.00
 Eye oint. 0.3% w/w (5 g) Rs. 7.00 - 8.00

Ciprofloxacin ☆

- I: This is the most widely used and one of the most effective quinolones. Bacterial spectrum includes gram negative organisms predominantly salmonella, shigella, campylobacter, neisseria and pseudomonas. Clinical indications include chloramphenicol resistant typhoid fever, meningococcal carrier state, typhoid carrier state,

2. Anti Infective Agents

gram negative osteomyelitis, invasive otitis media especially by *P. aeruginosa*, infection in neutropenic patients, respiratory infections, UTI, ear infection, septicemia, skin and soft tissue infection, gonorrhoea, eye infection including keratoconjunctivitis and blepharitis.

C/I: In pregnancy, children < 6 years, allergy.

P/C: Dose should be reduced in renal failure, with caution in CNS disorders, dehydration can lead to crystalluria.

S/E: GI disturbances-anorexia, nausea, vomiting and diarrhoea, CNS effects - confusion, agitation, hallucination and convulsions, cartilage damage in young children, leucopenia, allergic reactions - rash, pruritus, photosensitivity.

P/A: Tablet 100 mg, 125 mg, 250 mg, 500 mg, 750 mg

Infusion 2 mg/mL (100 mL)

Eye Drop 0.3% w/v (5 mL, 10 mL)

Eye ointment 0.3% w/w (5 g)

Combination preparation with tinidazole is also available.

Dose: 250 - 750 mg tablets b.d.

200 - 400 mg i.v. infusion b.d. over 30 - 60 minutes.

D/I: Same as for norfloxacin.

Cost:	Tab 250 mg	(10)	Rs. 30.00 - 50.00
	Inj 2 mg/mL	(100 mL)	Rs. 17.00 - 50.00
	Eye Drop 0.3% w/v	(5 mL)	Rs. 10.00 - 14.00
	Eye oint 0.3% w/w	(5 g)	Rs. 8.00 - 9.00

Cefloxacin

I: RTI, UTI, septicemia, osteomyelitis, meningitis, conjunctivitis, keratitis, corneal ulcers.

C/I: Hypersensitivity, pregnancy, lactation.

P/C: Use with caution in alcoholics, hepatic dysfunction. Avoid exposure to sunlight during treatment.

S/E: Photosensitivity, myalgia, thrombocytopenia, arthralgia, nausea.

P/A: Tablet 400 mg

Infusion 4 mg/mL

Eye Drops 0.3% w/v

Dose: 400 mg tablets b.d., slow i.v. infusion 400 mg diluted with 100-250 mL 5% dextrose normal saline over 1 h, b.d.

D/I: Same as for Norfloxacin.

Cost:	Tab 400 mg	(10)	Rs. 35.00 - 45.00
	Inj 400 mg	(100 mL)	Rs. 43.00 - 48.00
	Eye Drops 0.3% w/v	(5 mL)	Rs. 9.00 - 10.00

Cefloxacin

I: Gram negative infections, staphylococcal infections including multidrug resistant (*MRSA*), chlamydia or *Legionella*,

streptococci, mycoplasma, and mycobacteria.

C/I: Hypersensitivity to ofloxacin or quinolones, epilepsy or other seizure disorders, young children, pregnancy and lactation.

P/C: Impaired renal function or liver disease. Driving and operating of machinery to be avoided.

S/E: Similar to other qinolones, pseudomembranous colitis, headache, dizziness, tremor, convulsions, anxiety, depression, hallucination, disturbances in vision, smell and taste, hypotension during i.v. infusion, photosensitivity, haemorrhagic bullae, blood dyscrasias, anemia, leucopenia, thrombocytopenia, transient impairment of liver function, interstitial nephritis.

P/A: Tablet 100 mg, 200 mg

Infusion 2 mg/mL (100 mL).

Eye Drops 0.3% w/v

Dose: Oral: Lower urinary infections 200 mg daily

Upper UTI - 400 mg daily

Respiratory infection, ENT infection, skin and soft tissue infection - 400 - 600 mg daily

Infusion 200mg should be given i.v. over 30 min.

D/I: Same as for norfloxacin.

Cost:	Tab	100 mg	(10)	Rs. 105.00 - 125.00
	Inj	200 mg	(100 mL)	Rs. 81.00 - 85.00
	Eye Drops	0.3% w/v	(10 mL)	Rs. 19.00 - 20.00

Lomefloxacin

I: Similar to ciprofloxacin, skin infections, acute exacerbation of chronic bronchitis

C/I: Hypersensitivity, pregnancy

P/C: Use with caution in P.colitis, avoid exposure to sunlight, absorption is delayed by alcohol.

S/E: Nausea, headache, skin rash, diarrhoea, photosensitivity, dizziness

P/A: Tablet 400 mg

Dose: 400 mg o.d. for 10 - 14 days.

D/I: Same as for norfloxacin except that oral iron increases the absorption of lomefloxacin.

Cost :	Tab	400 mg	(10)	Rs. 90.00 - 110.00
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Sparfloxacin

I: Effective against gram positive, gram negative and anaerobic micro organisms, more potent against gram positive and gram negative organisms, chlamydia, rickettsia, mycoplasma, community acquired pneumonia, acute exacerbation of chronic bronchitis, sinusitis, gonococcal and non-gonococcal urethritis.

- C/I:** Hypersensitivity, pregnancy, lactation.
- P/C:** In severe renal insufficiency dosage should be reduced. It may produce false negative culture results for mycobacterium tuberculosis. Avoid exposure to sunlight and UV radiation.
- S/E:** Similar to other quinolones, pseudomembrane colitis, photosensitivity.
- P/A:** Tablet 100 mg, 200 mg
- Dose:** 2 tablets on day 1(400 mg)
Then 200 mg o.d. for 4 - 10 days.
Gonococcal urethritis - 200 mg single dose.
- D/I:** Do not combine with other agents causing QT prolongation - erythromycin, terfenadine, astemizole etc. Rifampicin reduces serum levels. Iron, antacids and milk reduces absorption.
Synergistic effect with tobramycin and vancomycin.
- Cost:** Tab 200 mg (6) Rs.150.00 - 180.00

Nalidixic Acid ✧

Nalidixic acid is the prototype of quinolones and has been in use for over five decades.

- I:** Effective against gram negative organisms especially E.coli, shigella, proteus. Less effective against pseudomonas, aerobactor, klebsiella. Used in chronic and acute urinary infection, intestinal infection such as dysentery and diarrhoea.
- C/I:** In pregnancy, convulsions, porphyria.
- P/C:** Cerebral atherosclerosis, seizures, parkinsonism, hepatic and renal impairment. Young children need reduced dose; avoid exposure to sunlight.
- S/E:** GIT disturbances- nausea, vomiting, diarrhoea; allergy-pruritus, rash, urticaria; fever, eosinophilia, photosensitivity, headache, drowsiness, myalgia, convulsions, haemolytic anaemia in those with G6PD deficiency.
- P/A:** Tablet 125 mg, 150 mg, 250 mg, 500 mg and 1 g
Suspension 300 mg/5 mL
Combination preparation with metronidazole is also available.
- Dose:** 1g q.d.s. for 1 - 2 weeks for adults.
- D/I:** Same as for norfloxacin.
- Cost:** Tab 500 mg (10) Rs.35.00 - 60.00
Susp 300 mg/5 mL (30 mL) Rs.15.00 - 25.00

2.2.9 MISCELLANEOUS ANTIMICROBIAL AGENTS

Lincomycin

- I:** It is a lincosamide antibiotic used in infections caused by susceptible organisms not responding to penicillin, acute and chronic osteomyelitis, respiratory tract infection, septic arthritis, endocarditis.

- C/I: Hypersensitivity, hepatic and renal impairment, endocrine and metabolic disorders.
- P/C: Monitor liver function test and blood count periodically, severe colitis may occur in patients with history of GI disorders.
- S/E: GIT - nausea, vomiting, pseudomembranous colitis; dizziness, headache, rash, pruritis, pica, vaginitis.
- P/A: Capsule 500mg
Syrup 125mg/5mL
Injection 300mg/mL
- Dose: Orally 500 mg t.d.s - q.d.s.; 600 mg 12 h i.m., i.v.
- D/I: Antacids and adsorbants reduces absorption, effect of neostigmine and pyridostigmine is antagonised, enhances effect of non depolarizing muscle relaxants such as tubocurarine.
- Cost: Cap 500 mg (10) Rs. 63.00 - 72.00
Syrup 125 mg / mL (60 mL) Rs. 45.00 - 50.00
Inj 300 mg/mL (2 mL) Rs. 16.00 - 34.00

Clindamycin

Semisynthetic derivative of lincomycin, generally bacteriostatic, bactericidal in high concentration.

- I: Intra abdominal abcess, pelvic abcess, peritonitis, lung abcess, acne vulgaris, malaria, encephalitis by toxoplasma, endocarditis, UTI. It can be used as an alternative to penicillin.
- C/I: Hypersensitivity, lincomycin meningitis.
- P/C: Chronic liver disease, renal disease, pregnancy, lactation
- S/E: Diarrhoea, pseudomembranous colitis, skin rash, Stevens Johnson syndrome, hepatic enzyme elevation, granulocytopenia, anaphylaxis, local thrombophlebitis, inhibit neuromuscular transmission, cardiac arrest with rapid i.v. infusion, oesophageal ulceration.
- P/A: Capsule 150 mg
Injection 150 mg/mL
Gel 1% w/w
- Dose: Adults - 150 to 300 mg 6 h.
Severe infections - 300 to 450 mg 6 h.
Parenteral 0.6 - 2.7 g/day slow i.v. infusion in 2 - 4 divided dose, can be given i.m. also.
- D/I: Same as for lincomycin.
- Cost: Caps 150 mg (4) Rs. 22.00 - 40.00
Inj 150 mg/mL (2 mL) Rs. 81.00 - 85.00

Vancomycin

- I: It is a glycopeptid antibiotic used in staphylococcal infection - severe infection esp. by MRSA, empyema, infective endocarditis, osteomyelitis, disseminated staphylococcal infection,

2. Anti Infective Agents

infections in patients with end stage renal disease(ESRD) or on hemodialysis or peritoneal dialysis, endocarditis due to enterococcus fecalis and in pseudomembranous colitis.

P/C: In severe hepatic and renal impairment .

S/E: Local thrombophlebitis, red neck syndrome characterised by sudden fall in B.P with or without maculopapular rash over the face and upper body. Generalized cutaneous rash caused by histamine release if administered rapidly i.v., ototoxicity - partly reversible sensorineural deafness, nephrotoxicity.

P/A: Tablet 50 mg
Injection 0.5 mg, 1 g

Dose: 500 mg - 1 g i.v. infusion over 30 minutes 12 h.
Pseudomembranous colitis - 125 to 500 mg 6 h, orally.

D/I: Antagonism of oral vancomycin by cholestyramine, increased risk of nephrotoxicity with amino glycosides and cephalosporins notably cephalothin, increased risk of ototoxicity with loop diuretics.

Cost:	Tab	50 mg	(10)	Rs. 70.00 - 72.00
	Inj	0.5 g	(vial)	Rs. 295.00 - 365.00

Teicoplanin

I: Active against gram positive bacteria especially MRSA, infective endocarditis due to gram positive organisms, in penicillin and cephalosporin allergic patients, peritonitis in patients on CAPD (continuous ambulatory peritoneal dialysis).

C/I: Renal failure, hypersensitivity, pregnancy and lactation.

P/C: Reduce dose in renal insufficiency.

S/E: Thrombophlebitis, pruritus, transient eosinophilia, allergic rashes.

P/A: Injection 200mg (vial)

Dose: 400 mg loading dose followed by 200 mg o.d., i.v. or i.m.

D/I: None reported.

Cost: Not freely available.

Fusidic Acid

I: Infections caused by penicillinases producing staphylococci, eradication of staphylococcal carrier state, bacterial endocarditis, septicemia, skin and soft tissue infection.

C/I: Pregnancy, lactation, hypersensitivity.

P/C: Oral dose should be increased due to incomplete absorption.

S/E: Skin rash, nausea vomiting, epigastric distress, acute peptic ulcers, rapid i.v. infusion can cause jaundice.

P/A: Injection 482 mg(base) vial
Tablet 240 mg(base)

Suspension 246 mg/5 mL

Ointment 2% w/w

Dose: Tablet - 480 mg(base) t.d.s., suspension - 738 mg(base) t.d.s.,
Parenteral - 482 mg(base) t.d.s., i.v. infusion.

D/I: None reported.

Cost: Not freely available.

Spectinomycin

I: Endocervical, rectal, urethral, and disseminated gonorrhea.

C/I: Pregnancy, lactation, hypersensitivity, infants.

P/C: Renal / hepatic impairment may occur.

S/E: Urticaria, chills, nausea, dizziness, insomnia.

P/A: Injection 2 g (vial)

Dose: 2-4 g single dose or 2 g b.d. for 3 - 5 days

D/I: None reported.

Cost: Not freely available.

Nitrofurantoin ★

I: Synthetic nitrofuran used in prevention and treatment of urinary tract infections. It is bacterio static, highly active in acid medium, effective against gram negative pathogens in urinary tract. eg. E.coli, klebsiella, enterococci, proteus, pseudomonas causing pyelitis, cystitis and post operative infections of urinary tract.

C/I: Severe renal impairment, G6 PD deficiency, infants less than 1 month, prophyria, pregnancy, hypersensitivity.

P/C: Chronic hepatic and renal disease, G6PD deficiency, diabetes mellitus.

S/E: Nausea, vomiting, diarrhoea, brown discoloration of urine, hypersensitivity reaction, chills, fever, leucopenia, hemolytic anemias in G6PD deficiency, cholestatic hepatitis, hepatocellular damage, chronic active hepatitis like disorder, pneumonitis with pulmonary infiltration and eosinophilia, intestinal pulmonary fibrosis, polyneuropathy with demyelination and degeneration of both motor and sensory nerves, benign intracranial hypertension, transient alopecia.

P/A: Tablet 50 mg, 100 mg

Suspension 25 mg/5 mL

Dose: Prophylaxis - 50 to 100 mg daily h.s.

Treatment - 200 to 400 mg daily in 4 divided doses for 14 days.

Children - 5 to 7 mg/kg/day in 4 divided doses.

D/I: Probenecid reduces excretion of nitrofurantion (risk of toxicity)

2. Anti Infective Agents

Cost:	Tab 50 mg	(10)	Rs. 4.00 - 5.00
	Susp 25 mg/5 mL	(60 mL)	Rs. 7.00 - 10.00

Mupirocin (pseudomonic acid)

I: Effective against gram positive and gram negative organisms, skin infection, impetigo folliculitis, eradication of staphylococcal carrier state.

C/I: Hypersensitivity

P/C: Avoid contact with eyes, pregnancy and lactation, increased risk of renal impairment if applied over large areas.

S/E: Burning, itching, dryness, contact dermatitis, cutaneous sensitization.

P/A: Ointment 2%w/w

Dose: Apply 3 times a day for 10 days.

D/I: None reported.

Cost: Oint 2 % w/w (5 g) Rs. 58.00 - 60.00

2.2.10 SULPHONAMIDES

Antimicrobials containing sulphonamide group are classified as those used systemically and those used for treatment of local GI infection. Sulphonamides except co-trimoxazole are rarely used now a days in the routine treatment of bacterial infection.

SULPHONAMIDES FOR SYSTEMIC INFECTION

1. Short acting

Sulphadiazine, sulphadimidine, sulphacetamide

2. Intermediate acting

Sulpha methoxazole

3. Long acting

Sulphamethoxy pyridazine

4. Ultra-long acting

Sulphadoxine, sulphametopyrazine.

SULPHONAMIDES FOR LOCAL INFECTION OF THE GUT

Sulphaguanidine, succinyl sulphathiazole, phthalyl sulphathiazole, salicylazo sulphapyridine (sulphasalazine).

I: Infection due to staphylococci, gonococci, pneumococci, clostridia, bacterioids, anthrax, H.influenzae, H.ducreyi, E.coli, shigella, Donovanias granulomatosis, nocardia, actinomyces, toxoplasma, chlamydia. Clinical indications include UTI uncomplicated by E.coli, toxoplasmosis, bacillary dysentery, shigellosis, chancroid, chemoprophylaxis of bacillary dysentery and meningitis, nocardiosis.

C/I: Sensitivity to sulfonamide, severe renal / hepatic impairment,

porphyria, SLE, lactation, pregnancy.

P/C : Renal insufficiency, elderly, blood dyscrasia, G6PD deficiency, AIDS, pregnancy.

S/E: Stevens Johnson syndrome, agranulocytosis, aplastic anemia, GI symptoms, hypersensitivity, crystalluria, thrombocytopenia, leukopenia.

P/A: Sulphadiazine Tablet 500 mg

Combination with trimethoprim is also available.

Silver-sulphadiazine Applicap 1%

Drops 1% w/v

Powder 1% (combination preparation)

Cream 1% (combination preparation)

Sulphacetamide Eye drops 10%, 20%, 30% w/v.

Sulphadoxin Tablet (combination preparation)

Suspension (combination preparation)

Sulphamoxole Tablet 500 mg

Sulphasalazine Enteric Tablet 500 mg

Dose : Sulphadiazine

Toxoplasmosis : 4 - 6 g/day, 6 h for 4-6 weeks.

Acute bacillary dysentery (shigellosis): initially 2 g followed by 1 g, 4-6 h for 1 week

Nocardiosis : 4 - 6 g/day for several months.

Sulphasalazine

Metabolised to 5-aminosalicylic acid and sulapyridine. It acts locally in the gut and has immunosuppressant properties, therefore used in rheumatoid arthritis as disease modifying agent : 0.5-1g, 4-6 h.

Silver sulphadiazine

1% cream to reduce microbial colonisation in burns.

D/I: Effect of thiopentone enhanced, effect of nicoumalone and warfarin enhanced, effect of sulphonylureas enhanced, antifolate effect and plasma concentration of phenytoin increased by sulphonamides, increased risk of antifolate effect with pyrimethamine, increased risk of nephrotoxicity, antifolate effect of methotrexate increased by sulphonamides.

Cost :	Sulphadiazine Tab 500 mg(10)	Rs. 14.00 - 15.00
	Silver sulphadiazine Drops 1% w/v(5 mL)	Rs. 15.00 - 17.00
	Cream 1%w/w(25g)	Rs.12.00 - 15.00
	Sulphacetamide Eye drops 20% (10 mL.)	Rs. 11.00 - 14.00
	Sulphamoxole Tab 500 mg(10)	Rs. 6.00 - 7.00
	Sulphasalazine Enteric Tab 500 mg (10)	Rs. 41.00 - 42.00

Co-trimoxazole (trimethoprim + Sulphamethoxazole) ♦

Co-trimoxazole is a combination of trimethoprim and sulphamethoxazole in the ratio 5 parts of sulphamethoxazole to 1 part of trimethoprim. These 2 drugs act on 2 steps of enzymatic pathway for synthesis

2. Anti Infective Agents

of tetrahydrofolic acid. Trimethoprim is a structural analogue of dihydrofolic acid.

- I: Antimicrobial spectrum include pneumococci, meningococci, *S. aureus*, *S. epidermidis*, *Salmonella*, *Strep. pyogenes*, viridans, *Proteus mirabilis*, *Brucella*, *Pasteurella*, *Nocardia*, methicillin resistant *S. aureus*. Clinical indications include acute uncomplicated UTI (except those by enterococci), prevention of recurrent UTI, shigellosis, typhoid fever, typhoid carrier, *Pneumocystis carinii* infection, *Isospora belli* diarrhoea, brucellosis, cyclosporiasis, donovanosis, listeriosis, legionellosis, non tuberculous mycobacterial skin diseases, pertussis, acute maxillary sinusitis and plague.
- C/I: Creatinine clearance < 15 mL/min, infants < 2 months, pregnancy at term and during lactation.
- P/C: Renal disease, history of hypersensitivity to sulphonamides, patients taking pyrimethamine, immunocompromised patients.
- S/E: Precipitates megaloblastic anaemia, leukopenia, thrombocytopenia, exfoliative dermatitis, Stevens Johnson syndrome, toxic epidermal necrolysis, nausea, vomiting, stomatitis, aplastic, haemolytic and macrocytic anemia, coagulation disorders, sulphahaemoglobinemia, nausea, crystalluria.
- P/A: Tablet 100/200 mg sulphamethoxazole + 20/40 mg trimethoprim.
400 mg sulphamethoxazole + 80 mg trimethoprim (Regular strength)
800 mg sulphamethoxazole + 160 mg trimethoprim (Double strength)
Suspension 200/400 mg sulphamethoxazole + 40/80 mg trimethoprim / 5 mL.
- Dose: Acute uncomplicated UTI : single dose treatment 1600 mg sulphamethoxazole + 320 mg trimethoprim
Prevention of recurrent UTI : T/S 80/400, o.d. or thrice a week
Shigellosis : 2 regular strength tabs b.d. for 5 days
To eradicate typhoid carriers : T/S 160/800 b.d. + rifamycin 400 mg/day, for 6 weeks.
Pneumocystis carinii infection : 100 mg/kg/day sulpha + 20 mg/kg/day trimethoprim in 2-3 divided doses for 14 days; for 21 days. In AIDS.
Prophylaxis - 1 double strength tab o.d. indefinitely.
Brucellosis : Along with rifampicin for 8 - 12 weeks.
Donovanosis : T/S 160/800 b.d. until lesions completely heal.
Non-tuberculous mycobacterial skin diseases : 160/800 b.d. for 3 months.
Pertussis : 8/40 mg/kg/d in 2 divided dose for 2 weeks.
Acute maxillary sinusitis : T/S 160/800 b.d. for 1-2 weeks.
- D/I: Effect of thiopentone enhanced, effect of nicoumalone and warfarin enhanced, effect of sulphonyl ureas enhanced, antifolate effect and plasma concentration of phenytoin increased by co-trimoxazole and possibly other sulphonamides, increased risk of antifolate effect

with pyrimethamine, increased risk of nephrotoxicity with cyclosporin. Antifolate effect of methotrexate increased by co-trimoxazole

Cost : Tab regular strength (10) Rs. 7.50 - 9.00
 Susp 200 S + 40 T (5 mL) Rs. 9.00 - 12.00

2.2.11 DRUGS USED IN LEPROSY

The causative organism of leprosy is acid fast bacilli mycobacterium leprae. It is a chronic granulomatous infection which mainly affects the skin, mucous membranes and nerves. Divided into multibacillary and paucibacillary types.

2.2.11.1 National Leprosy Eradication Program Classification

1. Lepromatous (LL) : Cutaneous manifestation is extensive, includes macule, papule plaques, ill defined borders with central part elevated later leonine facies.
2. Tuberculoid (TL) : Hypopigmented macule sharply demarcated, hypesthetic, margins become elevated and gyrate with central atrophic area.
3. Borderline lepromatous leprosy (BL)
4. Borderline tuberculoid leprosy (BT)
5. Indeterminate (IL) : cutaneous manifestation, anaesthetic patch.
 LL & BL : plenty of bacilli, multibacillary group.
 TL & BT : few bacilli, paucibacillary group.

Dapsone

Dapsone is chemically diaminodiphenyl sulfone. It is a folate antagonist and acts by inhibition of incorporation of PABA into folic acid. It's antibacterial action is antagonised by PABA. To prevent resistance, dapsone is combined with rifampicin for initial therapy.

- I: Leprosy, chloroquine resistant malaria, pneumocystis pneumonia in AIDS.
- C/I: Sulphone allergy, severe G6PD deficiency, severe anaemia, porphyria.
- P/C: Mild to moderate G6PD deficiency, sulphonamide allergy, moderate anaemia, cardiac and pulmonary disease, lactation and pregnancy.
- S/E: If daily dose exceeds 100 mg GI symptoms, fever, pruritus, rash, haemolysis, methaemoglobinemia, skin sensitization in dark people. Should not be used in patients with anemia and hypersensitivity to dapsone. It may precipitate reactions in leprosy.
- P/A: Tablets 25 mg, 50mg, 100mg.
- Dose: Multibacillary by multidrug: 100 mg/daily.
 Paucibacillary Leprosy : 100 mg daily for 6 months
- D/I: Not reported.
- Cost: Tab 50mg (1000) Rs. 40.00 - 42.00

Sulfoxone Sodium

Sulfoxone sodium is used in the treatment of leprosy. It is hydrolysed to dapsone in the GIT.

- I: Leprosy, dermatitis herpetiformis
- P/A: Tablet (enteric coated)
- Dose: 330 mg o.d. It is used when dapsone produces gastric irritation.
- Cost: Not freely available.

Rifampicin

- I: Bactericidal against *M.leprae*.
- Dose: Multibacillary by multidrug : 600mg/monthly under supervision, 99.9% bacilli killed in 3-7 days with rifampicin 600 - 1500 mg o.d. Paucibacillary leprosy : 600 mg/month for 6 months. Treatment should be continued till all the signs of activity has subsided. WHO is planning the combination of rifampicin + ofloxacin with the conventional regime of dapsone, rifampicin and clofazamine for multibacillary. Duration can be less than 6 months.

Clofazamine

Clofazamine has both antileprosy plus anti-inflammatory action. It is weakly bactericidal, binds to DNA and inhibit action, prevents the development of erythema nodosum leprosum. *M.leprae* has not developed resistance to clofazamine. Great advantage is its ability to make dapsone intolerant patient responsive to dapsone again.

- I: Leprosy
- C/I: First trimester of pregnancy, peptic ulcer, vomiting, diarrhoea and steatorrhea.
- P/C: Hepatic and renal impairment, function tests are required
- S/E: Reddish brown or black discoloration of skin, mucous membrane, urine and sweat. Eosinophilic enteritis.
- P/A: Capsule 50mg, 100mg
- Dose: 100 mg o.d. Multi bacillary by multidrug: 300 mg/monthly or supervised 50 mg daily. Treatment is recommended for 2 years.
- D/I: Not reported.
- Cost: Cap 50mg (100) Rs.113.00

Amithizone

- I: Tuberculoid leprosy, pulmonary tuberculosis.
- C/I: Liver and renal impariment, hypersensitivity, pregnancy, lactation.
- P/C: Use with caution in children and elderly.
- S/E: GI symptoms, hepatic damage, rash, vertigo, exfoliative dermatitis, Steven Johnson's Syndrome, leukopenia, agranulocytosis, thrombocytopenia, cerebral oedema.
- P/A: Not freely available.
- Dose: Leprosy 150 mg/day. Tuberculosis 150 mg/day for 4 weeks followed by 450 mg twice

weekly for 48 weeks along with other antituberculosis drug like INH and streptomycin.

D/I: Increased ototoxicity with streptomycin.

Ethionamide and Prothionamide

I: As a third line drug in the treatment of multibacillary leprosy

2.2.11.2 Treatment objectives

1. Control of lepra reactions.
2. Render *M. leprae* incapable of multiplication - to make the patient non effective.
3. Allow body to clear the bacilli.

2.2.11.3 Treatment of erythema nodosum leprosum (ENL) reaction

Anti pyretic and anti-inflammatory.

Prednisolone 60 - 120 mg/day.

Thalidomide 200 mg b.d. gradually reduced to 50 - 100 mg/day (contraindicated in pregnancy).

2.3 ANTI FUNGAL DRUGS

These drugs are used for superficial and systemic fungal infections.

2.3.1 Classification

I. ANTIBIOTICS

- A. Polyenes - Amphotericin B, Nystatin, Hamycin,
- B. Heterocyclic benzofuran - Griseofulvin.

II. ANTIMETABOLITE

Flucytosine (impaires the synthesis of fungal DNA)

III. AZOLES.

- A. Imidazoles (Topical) - Clotrimazole, Miconazole
(Systemic) - Ketoconazole
- B. Triazoles (Systemic) - Fluconazole, Itraconazole

IV. OTHER TOPICAL AGENTS.

Tolanaftate, undecylenic acid, terbinafine, ciclopiroxolamine, haloprogin, naftifine.

V. TERBINAFINE.

Amphotericin B ☆

It is described as the prototype of the polyene antibiotics

- I Oral, vaginal and cutaneous candidiasis and otomycosis, systemic mycoses especially for histoplasmosis, candidiasis, blastomycosis, cryptococcosis, paracoccidioidomycosis, coccidioidal meningitis, refractory cryptococcal meningitis. Reserve drug for persistance cases of kala azar - mucocutaneous leishmaniasis.

C/I: Hypersensitivity.

2. Anti Infective Agents

P/C: Chronic renal failure

S/E: Fever, chills, myalgia, nausea, vomiting, dyspnoea, reversible nephrotoxicity and anaemia, arrhythmias, neurological disturbances - hearing loss, diplopia, convulsions, peripheral neuropathy.

P/A: Topical application:

Tablet 100 mg

Injection 50 mg(vial)

Cream/Ointment 3%

Suspension 100 mg/mL

Other than injections other preparations are not freely available in India.

Dose: i.v. 0.5 to 0.7 mg/kg daily for 8 to 10 weeks. Infusions are given in 5 % dextrose over 2 to 4 h. For all patients it is advisable to give an initial 1 mg i.v. test dose followed by rapidly escalating doses.

Premedication with aspirin or paracetamol or the addition of hydrocortisone (25 mg) to the infusion decreases chills and fever. Saline infusions have been advocated to reduce azotemia.

Newer Formulations -

1. ABLC (amphotericin - B lipid complex).

Dose - 5 mg / kg daily.

Indication - refractory aspergillosis and other systemic mycosis.

2. ABCD (amphotericin B colloidal dispersion).

3. Ambisome (liposomal formulation available for i.v., less toxic).

D/I: Cyclosporin, pentamidine and other nephrotoxic agents increase toxicity, corticosteroids may enhance potassium depletion caused by the amphotericin-B, increased digitalis toxicity with digitalis glycosides, antagonises miconazole, enhances effect of curariform drugs.

Cost: Inj 50 mg (vial) Rs. 200.00 - 300.00

Nystatin ☆

It is similar to amphotericin-B in antifungal action. However, because of higher systemic toxicity, it is used usually for its local action.

I: Monilial vaginitis, conjunctivitis, corneal and cutaneous candidiasis, monilial diarrhoea.

C/I: Hypersensitivity.

P/C: Ineffective in dermatophytosis.

S/E: Rash, diarrhoea, nausea, vomiting

P/A: Tablet 5,00,000 units and 1,00,000 units.

Dose: Monilial vaginitis - 1,00,000 unit tab inserted b.d.

Monilial diarrhoea - 5,00,000 unit t.d.s.

Oral thrush - the tablets can be sucked or applied after powdering.

D/I: No known interactions.

Cost: Tab 5,00,000 (10) Rs. 50.00 - 51.00

Hamycin

Topical effective antifungal agent.

A fraction of the orally administered dose is absorbed but cannot be relied upon for the treatment of systemic mycosis.

- I: Topical application for oral thrush, cutaneous candidiasis, monilial and trichomonas vaginitis and otomycosis by aspergillus.

C/I: Hypersensitivity

P/C: Relatively safe.

S/E: Irritation, sensitization.

P/A: Suspension 10 mL
Ointment 5,00,000 units.

Dose: Local application thrice daily for 7 to 10 days.

D/I: None reported.

Cost: Susp 10 mL (2 mL) Rs. 16.00
Oint 5,00,000 units (5 g) Rs. 6.00 - 7.00

Griseofulvin ☆

It was one of the early antibiotics extracted from penicillium griseofulvum.

- I: Useful drug in the treatment of dermatophytosis - (ring worm infection) systemically. It is ineffective topically.

C/I: Porphyria, liver failure, hypersensitivity, systemic lupus erythematosus.

P/C: Small amounts may pass in breast milk, hepatic dysfunction. It decreases the efficacy of oral contraceptives and oral anticoagulants.

S/E: Headache, gastro intestinal disturbances, rash, photosensitivity, occasionally peripheral neuritis, transient leucopenia and albuminuria.

P/A: Tablet 125, 250 and 500 mg.

Dose: Adults: 125 - 250 mg q.d.s. with meals

Duration of therapy varies: skin-3 weeks, palm and soles - 4 to 6 weeks, finger nails - 4 to 6 months, toe nails - 8 to 12 months.

Children: 10 mg/kg daily.

D/I: Barbiturates reduce effect of griseofulvin, fatty meal enhances gastrointestinal absorption of griseofulvin. Reduced anti coagulant effect, reduced effect of oral contraceptives.

Cost: Tab 500 mg (10) Rs. 39.00 - 40.00

Flucytosine

It is a pyrimidine antimetabolite. The fungal selectivity depends on the fact that mammalian cells have a low capacity to convert inactive flucytosine into active 5 - fluorouracil.

- I: Cryptococcosis, candidiasis, chromoblastomycosis.

2. Anti Infective Agents

- C/I: Renal failure, hepatic impairments, blood dyscrasias, pregnancy and lactation.
- P/C: Renal dysfunction
Drug resistance appears rapidly when flucytosine is used alone.
- S/E: Dose dependent bone marrow depression, gastro intestinal disturbances, mild reversible hepatic dysfunction, rash, nausea, leucopenia, thrombocytopenia.
- P/A: Capsules 250 mg, 500 mg
- Dose: 100 - 150 mg/kg/day in 4 divided doses orally.
- D/I: Bone marrow toxicity of flucytosine enhanced by amphotericin B, cytarabine antagonises the action of flucytosine.
- Cost : Not freely available

Clotrimazole

It is an imidazole used for its local effect.

- I: Vulvovaginal, oral, oesophageal and cutaneous candidiasis, tinea versicolor, moderately severe ring worm infection of the skin, otomycosis, external ear fungal infection.
- P/C: May antagonise polyene antibiotics, avoid using during menses.
- C/I: 1st trimester of pregnancy, hypersensitivity.
- S/E: Rash, skin irritation, local burning or stinging.
- P/A: Vaginal tablets 100 mg, 200 mg, 500 mg
Gel 2 % w/w
Cream 1 % w/w
Lotion 1 % w/w
Powder 1 % (30 g, 60 g, 75 g)
Ear drops 1 % w/v.
- Dose: Pessaries - 100 - 500 mg per dose
Oropharyngeal candidiasis - 10 mg douche thrice daily.
Vaginal cream - one applicatorful (5g) per dose.
- D/I: Antagonism with polyene antibiotics.
- Cost:
- | | | | |
|-------------|---------|---------|-------------------|
| Vaginal tab | 100 mg | (6) | Rs. 15.00 - 23.00 |
| Powder | 1 % w/w | (75 g) | Rs. 26.00 - 27.00 |
| Cream | 1 % w/w | (15 g) | Rs. 20.00 - 25.00 |
| Lotion | 1% w/w | (30 mL) | Rs. 32.00 |
| Ear drops | 1 % w/v | (10 mL) | Rs. 10.00 - 20.00 |

Miconazole ☆

It belongs to imidazole group of drugs.

- I: Vulvovaginal and cutaneous candidiasis, tinea (pityriasis) versicolor, moderately severe ring worm infection of the skin.
- C/I: Hypersensitivity, pregnancy, lactation
- P/C: Monitor electrolyte and haemoglobin and during systemic

treatment.

S/E: Rash, gastro intestinal disturbances, fever, flushing, cramps.

P/A:	Ovules	200 mg
	Gel	2 % w/w
	Applicap	1 % w/v.
	Cream	2 % w/w
	Powder	2 % w/w
	Lotion	2 % w/v.

Dose: Topical - 2 % gel, 2 % powder, ointment, gel apply b.d. for 7 days
vulvovaginal candidiasis - 100 mg pessary at h.s. for 7 days.

D/I: Effect of anticoagulants, sulphonyl ureas and phenytoin enhanced.
It antagonises the effect other antifungals.

Cost:	Ovules	200 mg	(6)	Rs. 35.00 - 36.00
	Gel	2 % w/w	(20 g)	Rs. 27.00 - 28.00
	Applicap	1 % w/v	(30)	Rs. 28.00 - 29.00
	Powder	2 % w/w	(10 g)	Rs. 15.00 - 20.00
	Cream	2 % w/w	(10 g)	Rs. 18.00 - 20.00
	Lotion	2 % w/v	(15 mL)	Rs. 19.00 - 20.00

Ketoconazole ★

It was the first orally effective broad spectrum antifungal drug, useful in both dermatophytosis and deep mycosis.

I: Blastomycosis, histoplasmosis, paracoccidioidomycosis, chronic mucocutaneous candidiasis, esophageal candidiasis, disseminated coccidioidomycosis.

C/I: Pregnancy, lactation, cryptococcosis, malassezia, aspergillus and superficial inguinal.

P/C: Avoid contact with eyes. In case of sensitivity or severe irritation stop treatment.

S/E: Dose related nausea, anorexia, vomiting, idiosyncratic hepatotoxicity, dose related temporary endocrine effects - decreased adrenal cortical reserve, gynecomastia, decreased serum testosterone, libido and potency in males and menstrual irregularity in females. Pruritis and rash.

P/A:	Tablet	200 mg
	Shampoo	2 % w/w
	Cream	2 % w/w

Dose: Adults : 200 - 400 mg o.d.

Children > 2 yrs : 3.3 - 6.6 mg/kg/day o.d.

D/I: Increases cardiotoxicity of astemizole and terfenadine, enhances anticoagulant effect of warfarin, antacids reduce absorption.

2. Anti Infective Agents

metabolism accelerated by rifampicin (reduced plasma ketoconazole concentration), effect of anti coagulants enhanced, effect of phenytoin enhanced, reduced absorption of antimuscarinics, increases plasma cyclosporin concentration, histamine H₂ antagonists reduce absorption.

Cost:	Tab	200 mg	(10)	Rs. 60.00 - 140.00
	Shampoo	2% w/w	(50 mL)	Rs. 95.00 - 100.00
	Cream	2 % w/w	(15 g)	Rs. 46.00 - 48.00

For systemic infection prolonged treatment extending for several months may be required.

Itraconazole

This analogue of ketoconazole is superior to the parent compound in safety and efficacy.

- I: Blastomycosis, histoplasmosis, paracoccidioidomycosis, chronic mucocutaneous candidiasis, esophageal candidiasis, disseminated coccidioidomycosis, pseudallescheriasis, onychomycosis, sporotrichosis, cryptococcosis, aspergillosis.

C/I: Pregnancy.

P/C:, S/E:, D/I: Same as for ketoconazole

P/A: Capsules 100 mg

Dose: 200 mg o.d./b.d. oral with food (to enhance absorption)

Oropharyngeal candidiasis - 15 days

Vulvo vaginal candidiasis - 1 day.

Pityriasis versicolor - 7 days

Onychomycosis - 3 months

Cost: Cap 100 mg (4) Rs. 137.00 - 180.00

Fluconazole

It is a water soluble triazole.

- I: Oropharyngeal, esophageal and vulvovaginal candidiasis, catheter acquired candidemia, initial and maintenance therapy for cryptococcal meningitis, maintenance therapy in coccidioidal meningitis, in the initiation of the preparative regimen for bone marrow transplant to decrease the incidence of deep candidiasis among recipients of allogenic bone marrow transplants.

C/I: Hypersensitivity, Pregnancy, lactation, age below 4 weeks.

P/C: In hepatic and renal dysfunction.

S/E: Nausea, abdominal distress, allergic rash especially in patients infected with HIV, Steven Johnson's Syndrome, reversible alopecia, and rarely anaphylaxis, hepatic necrosis, neutropenia.

P/A: Tablet 50 mg, 100 mg, 150 mg, 200 mg

Capsule 50 mg, 100 mg, 150 mg, 200 mg

Injection 200 mg

Dose: Adults: mucosal - 50 to 100 mg / day increased to 200-400 mg day

Maintenance to prevent relapse of cryptococcal meningitis: 100-200 mg / day

i.v. infusion : 5 - 10 mL / min.

Children: 3 - 6 mg / kg/day for systemic infections, maximum 12 mg/kg/day

D/I: Same as ketoconazole. It increases the serum level of phenytoin, warfarin and sulfonylureas.

Cost :	Tab	100 mg	(4)	Rs. 74.00 - 92.00
	Caps	50 mg	(4)	Rs. 40.00 - 44.00
	Inj	200 mg	(100 mL)	Rs. 59.00 - 75.00

2.3.2 Other Topical Antifungals

Ciclopiroxolamine, haloprogin, terbinafine, naftidine has same spectrum as imidazoles. Tolnaftate and undecenoic acid are effective against ringworm but not candidiasis.

Terbinafine

New systemic antifungal

I: Onychomycosis, ring worm

C/I: Hypersensitivity

P/C: It increases cyclosporine levels

S/E: Most common - gastro intestinal distress Rash, hepatitis, pancytopenia - reported.

P/A: Tablet 250 mg
Cream 10 mg/g

Dose: 250 mg oral o.d.

D/I: Drugs that induce or inhibit microsomal enzymes may interfere with terbinafine metabolism.

Cost:	Tab	250 mg	(14)	Rs. 1247.00 - 1250.00
	Cream	10 mg / g	(10 g)	Rs. 165.00 - 173.00

2.4 ANTIVIRAL DRUGS

The use of antiviral compounds for chemotherapy and chemoprophylaxis of viral diseases is a new development in the field of infectious diseases. General antiviral drugs used for curative and prophylactic therapy have been introduced during the past two decades.

2.4.1 Classifications

I. FOR HERPES GROUP VIRUSES.

Acyclovir, valacyclovir, ganciclovir, famciclovir, penciclovir, foscarnet.

II. FOR RETROVIRUSES

a. Nucleoside reverse transcriptase inhibitors.

Zidovudine, zalcitabine, stavudine, lamivudine

b. Non nucleoside reverse transcriptase inhibitors

Nevirapine, delaviridine

c. Protease inhibitors

Saquinavir, indinavir, ritonavir.

III. FOR INFLUENZA A VIRUSES

Amantidine, rimantidine, ribavirin.

IV. NON SELECTIVE

Human interferons

Acyclovir ✧

Acyclovir is a highly potent and selective inhibitor of the replication of certain herpes viruses. It is ineffective in cytomegalovirus infections. Valacyclovir, the L-valyl ester of acyclovir, is almost entirely converted to acyclovir after oral administration.

I: Cerebral HSV infections, treatment of mucocutaneous herpes simplex virus infections in immuno-compromised hosts, reduction of frequency of HSV-associated disease in immunosuppressed patients, HSV encephalitis, herpes zoster in immunocompromised patients, Zoster-associated pain, Herpes zoster ophthalmicus, normal children with chicken pox.

C/I: Glaucoma, psychiatric disease, depression, hypersensitivity.

P/C: Pregnancy, nephrotoxic agents with acyclovir may cause further nephrotoxicity.

S/E: Renal dysfunction, nausea, vomiting, central nervous system changes - lethargy and tremors.

P/A: Tab 200 mg, 400 mg, 800 mg

Inj 250 mg vial

Cream 5% w/w

Dose: Adults: Oral -HSV : 200 mg 5 times daily for 5 days

Herpes zoster : 800 mg 5 times daily for 7 days, prophylaxis - 200 mg q.d.s.

Children: Herpes zoster / mucocutaneous herpes simplex : 5 mg/kg/dose 8 h for 7 days, prophylaxis - 200 mg q.d.s.

Parenteral - Herpes simplex encephalitis : 10 mg/kg/dose 8 h i.v infusion for 10-14 days 8 h

Varicella zoster infection : 10 mg/kg/dose 8 h for 7 days

D/I: Extreme lethargy is reported after administration of zidovudine with i.v. acyclovir. Probenecid reduces acyclovir excretion leading to increased plasma concentration.

Cost: Tab 200 mg (10) Rs. 52.00 - 200.00

Inj i.v. 250 mg (vial) Rs. 400.00 - 1041.00

Cream 5% w/w (5 g) Rs. 30.00 - 35.00

Ganciclovir

Ganciclovir is an analogue of acyclovir

- I: Treatment of cytomegalovirus retinitis in immunosuppressed patients, prevention of cytomegalovirus (CMV) disease in organ transplant recipient, treatment of CMV-associated syndromes - pneumonia, oesophago-gastrointestinal infections, hepatitis, "wasting illness"
- C/I: Pregnancy, neutropenia.
- P/C: Additive bone marrow suppression with zidovudine.
- S/E: Bone marrow suppression especially neutropenia.
- P/A: Capsules 250 mg
Injection 500 mg(vial)
- Dose : Oral: 1 g t.d.s.
Parenteral : i.v. 5 mg/kg every 12 h for 14 to 21 days followed by a maintenance dose of 5 mg/kg i.v. per day or 5 times per week, possibly for as long as immunosuppression exists.
- D/I: Increased risk of myelosuppression with zidovudine and other myelosuppressive drugs.
- Cost : Not commercially available.

Foscarnet

It is a drug that does not require phosphorylation to exert its antiviral activity.

- I: Cytomegalovirus retinitis in AIDS, acyclovir-resistant HSV and VZV, ganciclovir-resistant CMV infections.
- C/I: Anaemia, dehydration, renal function impairment.
- P/C: Monitor renal function closely. Monitor mineral and electrolyte changes against seizures.
- S/E: Renal impairment, hypocalcemia, hypomagnesemia, hypokalemia, hypophosphatemia.
- P/A: Injection 24 mg /mL(250 mL, 500 mL)
- Dose: i.v. 60 mg/kg every 8 hrs for 14 to 21 days followed by a maintenance dose of 90 to 120 mg/kg o.d.
- D/I: Nephrotoxic drugs like aminoglycosides and amphotericin B cause increased risk of nephrotoxicity. Concurrent use with zidovudine increases anaemia. Concurrent use with intravenous pentamidine may result in severe but reversible hypocalcemia, hypomagnesemia and nephrotoxicity.
- Cost : Not freely available.

Zidovudine

It is a reverse transcriptase inhibitor that has been shown to prolong survival, decrease the frequency and severity of opportunistic infections and decrease the rate of perinatal transmission of HIV-1 infection.

- I: Zidovudine is most appropriately used as part of combination antiretroviral therapy for patients with HIV infection and with

2. Anti Infective Agents

less than 500 CD4+ T Cells per microliter.

The use of zidovudine monotherapy is currently restricted to the prevention of maternal - foetal transmission of HIV.

C/I: Hypersensitivity

P/C: Patients starting therapy should be monitored for toxicity at least every other week for the first month and then monthly. Chronic hepatic or renal dysfunction.

S/E: Fatigue, malaise, nausea, headache, bone marrow suppression, proximal myopathy, cardiomyopathy, bluish discoloration of nails

P/A: Capsules 100 mg

Injection 200 mg / 20 mL

Dose: Adult: 200 mg three times a day, oral in combination with other antiretroviral agents.

Children: > 3 months - 12 to 22 mg/kg/day in divided dose, 6 h

Not recommended under the age of 3 months

D/I: Increased risk of toxicity with other nephrotoxic and myelosuppressive drugs.

Extreme lethargy is reported with i.v. acyclovir, profound myelosuppression with ganciclovir. Probenecid increases plasma zidovudine concentration.

Cost: Cap 100 mg (10) Rs. 250.00 - 550.00
Injection available on special request.

Amantidine and rimantadine

These are primary synthetic amines which inhibit replication of Influenza A.

I: Prophylaxis and treatment of Influenza A in adults, particularly elderly and prophylaxis in susceptible children.

C/I: Hypersensitivity

P/C: Chronic hepatic dysfunction, chronic renal dysfunction, peptic ulcer, epilepsy, eczema.

S/E: Dizziness, anxiety, insomnia, difficulty in concentrating, seizures and worsening of congestive heart failure.

P/A: Capsules 100 mg

Syrup 50 mg/5 mL

Dose: Adult : 100 to 200 mg / day orally for 5 to 7 days

Prophylaxis : 100 to 200 mg/day orally daily for the peak duration of the outbreak.

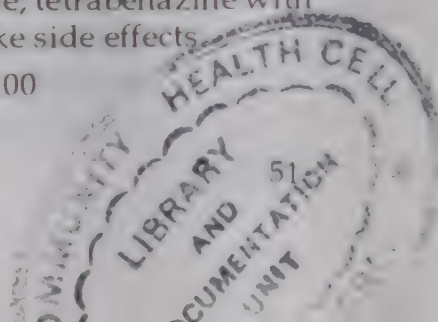
Children (1- 9 years) : 5-9 mg/kg/day o.d.

D/I: Concurrent use of antihypertensives, antimuscarinics, antipsychotics, domperidone, metoclopramide, tetrabenazine with amantidine potentiates the anticholinergic-like side effects.

Cost: Cap: 100 mg (10) Rs. 30.00
Syrup: Not freely available.

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Ribavirin

Ribavirin is a synthetic nucleoside analogue that inhibits a wide range of RNA and DNA viruses.

- I: Respiratory syncytial virus infections, para influenza virus infections in children, influenza A and B virus infections in young adults, hepatitis B virus, lassa fever, haemorrhagic fever with renal syndrome caused by Hantaan virus, argentinian hemorrhagic fever, treatment and prophylaxis of Congo-Crimean haemorrhagic fever

C/I: Pregnancy, hypersensitivity.

P/C: Renal impairment, asthma, anemia

S/E: Haematopoietic toxicity, bronchospasm, rash, conjunctival irritation, mutagenic, teratogenic, embryotoxic.

P/A: Capsules 100 mg, 200 mg

Syrup 50 mg/mL

Dose: Adults : 200 mg t.d.s. or q.d.s. orally,

Children : 10 mg / kg / day in divided doses.

Cost: Cap 200 mg (4) Rs. 220.00 - 225.00

Syrup 50 mg / 5 mL (30 mL) Rs. 80.00 - 90.00

Interferon

Interferon are cytokines that exhibit a broad spectrum of antiviral activities as well as immuno modulating and antiproliferative properties. There are several types of interferons produced by different tissues - Alpha, Beta and Gamma.

- I: Intranasally for prophylaxis of rhinovirus infections, intra lesionally and systemically for treatment of genital warts (interferon Alpha-2b, Alpha-n1), treatment of chronic Hepatitis B virus (interferon Alpha-2b), treatment of chronic hepatitis non A, non B/C infection (interferon Alpha-2b), treatment of hairy cell leukaemia (interferon Alpha-2a, Alpha-2b), chronic granulomatous disease (interferon Alpha-1b).

C/I: Hypersensitivity

P/C: It increases the effects of theophyllines.

S/E: Headache, lethargy, fever, neurotoxicity - numbness, neuropathy and tremor, digestive disturbances, alopecia.

P/A: Injection Alpha-2a 3, 9 and 18 million units/vial

Alpha-2b 3, 5, 10 and 30 million units/vial

Alpha-n1 3 and 10 million units/vial

Dose: Interferon Alpha-2b in chronic HBV infection - 5 million units daily for 16 weeks.

Interferon Alpha-2b in chronic non-A non-B / C infections hepatitis.- 3 million units three times a week for 6 months.

Interferon Alpha-2a - individualised based on the patient

2. Anti Infective Agents

D/I: Concurrent use of myelosuppressive drugs increases bone marrow toxicity, concurrent use of interferon with sedatives like anti-anxiety drugs, antihistamines and antidepressants potentiates the sedative effects. On concurrent use the effect of theophylline is occasionally enhanced.

Cost: Inj Alpha-2a (3 million units) Rs. 1000 (M) - 1350 (G)

Other preparations are not freely available.

2.5 ANTIPARASITIC AGENTS

2.5.1 Antiprotozoal drugs

2.5.1.1 Antimalarial drugs

Malaria is a protozoan disease. The common parasites are *Plasmodium vivax* and *P. falciparum*.

Drugs used for the treatment

1. 4-Aminoquinolones: Chloroquine, amodiaquine, hydroxychloroquine
2. Dihydrofolate reductase inhibitors: Pyrimethamine, proguanil.
3. 8-Aminoquinolones: Primaquine
4. Quinine and structurally related compounds: Quinine, quinidine, mefloquine.
5. Quinghaosu derivatives: Artesunate, artemether.
6. Miscellaneous: Sulphadoxine, halofantrine.

Chloroquine

1. It is highly effective against asexual erythrocytic form of *P. vivax* and sensitive strains of *P. falciparum*. There is no action on the exoerythrocytic stage or on gametocytes. It is also used in rheumatoid arthritis, extraintestinal amoebiasis, lupus erythematosus, porphyria.

C/I: Hypersensitivity, G6PD deficiency, pregnancy, lactation.

P/C: Prolonged use may cause reversible lichenoid skin eruptions, use with caution in hepatic or renal dysfunction, epilepsy and psoriasis.

S/E: GI symptoms - nausea and vomiting, visual disturbances, headache, peripheral neuropathy, toxic myopathy, keratopathy and psychiatric illness. If retinopathy occurs this may progress and worsen even if the drug is withdrawn. Keratopathy may regress on stopping the drug.

P/A: Tablet 100 mg, 250 mg, 500 mg

Injection 40 mg/mL, 64.5 mg/mL

Suspension 160 mg/10 mL

Dose : Treatment - 600 mg + 300 mg (6 h later) followed by 300 mg o.d. for following two days. In the majority of cases caused by sensitive strains of *P.falciparum* this course is sufficient to suppress the attack. For *P.vivax* follow up therapy with 8-aminoquinolones is mandatory in order to destroy the exoerythrocytic form or the parasite which leads to relapse.

Prophylaxis - 300 mg o.d. once a week starting 2 weeks before entering an endemic area, continuing for 4 weeks after leaving.

D/I: Antacids reduce absorption, levels of digoxin in blood may be increased, other antimalarials antagonise chloroquine.

Cost :	Tab	250 mg	(10)	Rs. 3.00 - 10.00
	Inj	64.5 mg/mL	(5 mL)	Rs. 1.50 - 4.00
	Susp	160 mg/10 mL	(60 mL)	Rs. 6.50 - 13.00

Pyrimethamine

I: Chloroquine resistant *falciparum* malaria (used only in combination with dapson or sulphadoxine); toxoplasmosis.

C/I: Anaemia, bone marrow depression, hypersensitivity, seizure disorders.

P/C: Use with caution in hepatic and renal impairment, G6PD deficiency and severe allergy or asthma.

Folinic acid should be supplemented when given in pregnancy, blood counts required with prolonged treatment.

S/E: Rash, loss of appetite, gastric irritation, insomnia, sore throat, fever and unusual bleeding.

P/A: All preparations contain pyrimethamine 1 part plus sulfadoxine 20 parts.

Tablet (pyr 12.5, 25, 37.5, 50 mg + sulpha 250, 500, 750, 1000 mg)

Suspension (pyr 12.5, 25 mg + sulpha 250, 500 mg per 5 mL)

Dose : Acute malarial attack - 2 to 3 tablets (pyrimethamine 25 mg + sulphadoxine 500 mg) single dose on day 3 of quinine therapy.

Prophylaxis - 1 tablet weekly

D/I: Concurrent use of pyrimethamine with bone marrow depressants may increase the leukopenic and thrombocytopenic effects. Increased anti folate effect with methotrexate.

Cost :	Tab (pyr 25 mg + sulpha 500mg)	(2)	Rs. 4.00 - 6.00
	Susp(pyr 12.5 mg + sulpha 250 mg/ 5 mL)	(10 mL)	Rs. 5.00 - 7.00

Proguanil

I: Prophylaxis of *falciparum* malaria.

C/I: Hypersensitivity, severe renal failure, known resistance of plasmodium species.

P/C: Pregnancy demands folate supplementation. Use with caution during lactation. Proguanil distorts results of *falciparum* drug sensitivity tests.

2. Anti Infective Agents

- S/E: GI disturbances, vertigo, headache, rash, hair loss, haematological abnormalities in patients with renal impairment
- P/A: Tablet 100 mg
- Dose: Prophylaxis 200 mg daily, for travellers start 1 week before travel and continue for atleast 4 weeks after leaving the endemic area
- D/I: None reported
- Cost: Tab 100 mg (10) Rs. 24.00 - 25.00

Primaquine

- I: It is highly effective against the exoerythrocytic stage of *P. vivax* and against gametocyte of *P. falciparum* and all species of plasmodia.
- C/I: Rheumatoid arthritis, G6PD deficiency, SLE, hypersensitivity, pregnancy, lactation, concurrent administration of haemolytic drugs.
- P/C: Conduct routine blood examination during the course of therapy.
- S/E: GI symptoms, haemolytic anaemia, methaemoglobinemia, granulocytopenia, agranulocytosis.
- P/A: Tablet 2.5 mg, 7.5 mg and 15 mg
- Dose: 15 mg o.d. for 2 weeks
- D/I: Inhibits metabolism of chloroquine. Haemolytic drugs (sulfonamides) and bone marrow suppressants (methotrexate, chloramphenicol) potentiates toxicity of primaquine
- Cost: Tab 7.5 mg (10) Rs. 7.00 - 15.00

Quinine

- I: Acts on mature trophozoites of all species of plasmodium.
- C/I: Hypersensitivity, G6PD deficiency, pregnancy, lactation
- P/C: Use with caution in chronic renal dysfunction, optic neuritis, myasthenia gravis, cardiac dysfunction
- S/E: Cinchonism - tinnitus, nausea, headache and disturbed vision, GI symptoms, angioedema, hyperinsulinemic hypoglycemia, excitement, delirium, thrombocytopenia, agranulocytosis, hypotension, muscle paralysis in myasthenic patients.
- P/A: Tablet 100 mg, 150 mg, 300 mg, 600 mg.
Injection 300 mg/mL
- Dose: Adult : 300 - 600 mg t.d.s. for 5 - 7 days.
Children : 25 mg/kg/day 8 h, for 7 days.
- D/I: Blood levels of digoxin increased, hypoprothrombinemic effect of warfarin enhanced, cimetidine inhibits quinine metabolism, hypoglycemic effect of oral antidiabetics enhanced.
- Cost: Tab 300 mg (10) Rs. 35.00 - 60.00
Inj 300 mg/mL (2 mL) Rs. 11.00 - 19.00.

Mefloquine

- I: Prevention and treatment of chloroquine resistant and multidrug resistant *P. falciparum* malaria. Prophylaxis for non-immune travellers staying for short duration in endemic zones.
- C/I: Hypersensitivity, pregnancy, lactation and history of convulsions or psychiatric illness.
- P/C: Use with caution in cardiovascular disorders, hypertension, coagulation disorders, epilepsy, hepatic or renal impairment. Avoid alcohol during treatment as it may cause increased adverse effect.
- S/E: Nausea, vomiting, diarrhoea, dizziness, itching, rash, hallucination and depression.
- P/A: Tablet 250 mg
- Dose: Multi-drug resistant case : 15-25 mg/kg b.w. (750-1000 mg single dose).
Prophylaxis :250 mg weekly one week before entering an endemic area and for 4 weeks after leaving.
- D/I: Increased risk of convulsions with chloroquine, ECG abnormalities with beta blockers and halofantrine, potentiation of cardiotoxicity and neurotoxicity with quinine, increased metabolism of valproic acid, decreased metabolism of mefloquine with ketoconazole.
- Cost : Tab 250 mg (2) Rs. 90.00 - 100.00

Artemether

Artemether is a semisynthetic antimalarial agent derived from artemisinin from *artemisia anua*, also known as qinghausu, a plant used in Chinese medicine.

- I: It has got schizonticidal activity against asexual forms of *P. falciparum* and *P. vivax*. Effective against all strains resistant to other antimalarial agents. Used in severe complicated *falciparum* infection including cerebral malaria.
- C/I: Hypersensitivity, pregnancy.
- P/C: Avoid concomitant use of drugs causing ECG abnormalities and constantly monitor such patients.
- S/E: GI symptoms, bradycardia, AV block, reduced leucocyte and reticulocyte counts, nausea, vomiting, transient increase in serum transaminases.
- P/A: Injection 80 mg
Capsules 40 mg
- Dose: Adult :80 mg b.d. on day 1 followed by 80 mg o.d. for next 4 days.
Children : 1.6 mg/kg b.d. on day 1 followed by 1.6 mg/kg o.d. for next 4 days.
- D/I: Antagonises pyrimethamine, synergism with mefloquine, primaquine and tetracyclines. ECG abnormalities with quinidine, terfenadine, amiodarone, tricyclic antidepressants and some phenothiazines.
- Cost : Inj 80 mg (6 x 1 amp) Rs. 1290.00
Other preparations are not freely available in India

Halofantrine

- I:** Mild to moderate acute malaria caused by susceptible strains of *Plasmodium falciparum* and *P. vivax*
- C/I:** Arrhythmia, hypersensitivity, thiamine deficiency
- P/C:** Pregnancy and lactation. Regular visit to physician to check progress, avoiding exposure to mosquitoes, especially at peak feeding times (between dusk and dawn)
- S/E:** Acute intravascular haemolysis, cardiovascular toxicity, gastrointestinal disturbances.
- P/A:** Tablet 250 mg
Suspension
- Dose:** Oral 500mg taken on an empty stomach 6 h t.i.d. for one day. Treatment should be repeated after one week.
- D/I:** Concomitant use with mefloquine may potentiate the adverse cardiac effects.
- Cost:** Not freely available.

Properties of antimalarial drugs

Drugs	Pharmacokinetic Properties	Antimalarial Activity	Minor Toxicity	Major Toxicity
Quinine, quinidine	Good oral and i.m. absorption; Cl and Vd reduced, but plasma protein binding (principally) to a 1 acid glycoprotein) increased (90%) in malaria; $t_{1/2}$: 16 h in malaria, 11 h in healthy persons.	Acts mainly on trophozoite blood stage; kills gametocytes of <i>P. vivax</i> , <i>P. ovale</i> & <i>P. malariae</i> , no action on liver stages.	Common: Cinchonism: tinnitus, high-tone hearing loss, nausea, vomiting, Postural hypotension, syndrome, ECG QTc interval prolongation. Rare: Diarrhoea, visual disturbances, rashes. Note: Bitter taste.	Hypotension, arrhythmia, thrombocytopenia, haemolysis, uremia, cholestatic Hepatitis, cardiotoxic.
Chloroquine	Good oral absorption, very rapid and absorption complex pharmacokinetics; enormous Cl and Vd. Blood concentration profile determined by distribution processes in malaria $t_{1/2}$ 1-2 months	As for quinine but more rapid.	Common: Nausea, dyspepsia, pruritus in dark skinned persons, postural hypotension. Rare: Accommodation difficulties, rashes. Note: Bitter taste, well tolerated	Hypertensive shock, cardiac arrhythmias, neuropsychiatric reactions. Retinopathy, skeletal cardiac myopathy

KERALA STATE DRUG FORMULARY, April - 1999

Mefloquine	Adequate oral absorption; As for quinine no parenteral preparation; $t_{1/2}$: 14-20 days (shorter in malaria)		Nausea, giddiness, dysphoria, confusion, sleeplessness, nightmares	Neuropsychiatric reactions, convulsions, / encephalopathy
Tetra-cycline, doxycycline	Excellent absorption; $t_{1/2}$: 8h for tetracycline, 18h for doxycycline	Weak antimalarial activity; should not be used alone for treatment	Gastrointestinal intolerance, deposition in growing bone and teeth, photosensitivity, moniliasis, benign intracranial hypertension	Renal failure
Halofan-trine	Highly variable absorption; $t_{1/2}$: 1-3 days (active desbutyl metabolite $t_{1/2}$: 2-7 days)	As for quinine but more rapid	Diarrhoea	Prolonged QT interval, AV conduction delay
Artemisinin and derivatives (artemether, artesunate)	Good oral absorption, variable absorption of IM artemether; artesunate and artemether biotransformed to active metabolite dihydroartemisinin; all drugs eliminated rapidly	Broader stage specificity and more rapid than other drugs; no action on liver stages	Reduction in reticulocyte count; fever	Neurotoxicity not reported in human
Pyrimetha-mine	Good oral absorption; variable IM absorption; $t_{1/2}$: 4 days	For blood stages acts mainly on mature forms; causal prophylactic	Well tolerated	Megaloblastic anaemia, pancytopenia, pulmonary infiltration
Proguanil (chloro-guanide)	Good oral absorption; biotransformed into active metabolite cycloguanil; $t_{1/2}$: 16h	Causal prophylactic; not used for treatment	Well tolerated with mouth ulcers and rare alopecia	Megaloblastic anaemia
Primaquine	Complete oral absorption; active compound not known; $t_{1/2}$: 2-7h	Radical cure; some activity against blood stage infection; used to eradicate exoerythrocytic (hepatic) forms of <i>P. vivax</i> and <i>P. ovale</i> and to prevent relapses; kills gametocytes of <i>P. falciparum</i>	Nausea, vomiting, diarrhoea, abdominal pain, haemolysis methaemoglobinaemia	Massive haemolysis in G6PD deficiency

Prophylaxis and self-treatment for malaria

Drug	Usage	Adult Dosage	Child Dosage
Prophylaxis			
Mefloquine	used in areas where chloroquine-resistant malaria has been reported	225 mg of base (250 mg of salt) orally, once per week	<15 kg: 4.6 mg base 15-19 kg: 1/4 tab/ week 20-30 kg: 1/2 tab/ week 31-45 kg: 3/4 tab/ week >45 kg: 1 tablet/ week
Doxycycline	used as alternative to mefloquine.	100 mg orally, o.d.	>8 years of age 2 mg/ kg/ day orally
Chloroquine	used in areas where chloroquine-resistant malaria has not been reported	300 mg of base (500 mg of salt)	5 mg of base/ kg/ week orally, once per week orally, maximum upto 300 mg of base
Proguanil	used simultaneously with chloroquine as alternative to mefloquine or doxycycline	200 mg orally, o.d., in combination with weekly chloroquine as	<2 years: 50 mg/ day 2-6 years: 100 mg/ day 7-10 years: 150 mg/ day >10 years: 200 mg/ day
Primaquine	used for travellers only after testing for G6PD deficiency; postexposure prevention for relapsing malaria	15 mg of base (26.3 mg of salt) orally, o.d for 14 days	0.5 mg of base/ kg orally for 14 days
Self-treatment			
Pyrimethamine-sulfadoxine	In areas with chloroquine resistant malaria, should be carried during travel by persons taking mefloquine or doxycycline.	3 tablets (75 mg of pyrimethamine and 1500 mg of sulfadoxine) orally, as a single dose	5-10 kg: 1/2 tablet 11-20 kg: 1 tablet 21-30 kg: 1 1/2 tablet 31-45 kg: 2 tablets >45 kg: 3 tablets

2.5.1.2 Other antiprotozoal agents**2.5.1.2.1 Drugs for leishmaniasis**

Drugs used in the treatment of Leishmaniasis are

ANTIMONIALS

Sodium stibogluconate, Meglumine, Urea stibamine

DIAMIDINES

Pentamidine, Hydroxy stilbamidine

MISCELLANEOUS DRUGS

Amphotericin B, Ketoconazole, Allopurinol

Sodium Stibogluconate ☆

I: Drug of choice for kala azar

C/I: Pneumonia, myocarditis, nephritis, hepatitis.

P/C: i.v. injection must be given slowly and stopped if coughing or substernal pain develops, i.m. is painful.

S/E: Nausea vomiting, metallic taste in the mouth, pain, stiffness of injected muscle, sterile abscess, ECG abnormalities, elevation of hepatic transaminases.

P/A: Injection (equivalent to total antimony 100 mg) 30 mL(vial).

Dose: 20 mg/kg daily i.m. or i.v. injection for 20 - 30 days or more.

D/I: Concurrent use with nephrotoxic drugs increases nephrotoxicity.

Cost: Not freely available.

Pentamidine ☆

I: Active against *L. donovani*, *pneumocystis carinii*, kala azar - salvage therapy of antimony failure cases, *pneumocystis pneumonia* in AIDS patients and trypanosomiasis.

C/I: Impaired renal function.

P/C: Reduce dose in renal failure, risk of hypotension, monitor kidney/ liver function, blood glucose, blood count and ECG.

S/E: Toxicity is due to histamine release. Hypotension, palpitation, fainting, vomiting, rigor and fever after i.v. injection, kidney and liver damage, cardiac arrhythmias, hypoglycemia, hyperglycemia, pancreatitis, neutropenia, unpleasant metallic taste, nausea, headache, anxiety.

P/A: Pentamidine isothionate injection 300 mg (vial).

Dose: 4 mg / kg i.v. infusion over 1-2 hours on alternate days, total 12-15 injections

D/I: Abnormal haematological effect with bone marrow depressants. increased risk of pancreatitis with didanosine, increased risk of torsades de pointes with erythromycin, reversible hypocalcemia, hypomagnesemia and nephrotoxicity with foscarnet.

Cost: Not freely available.

Other drugs used in resistant cases

1. Amphotericin - B
2. Ketoconazole
3. Allopurinol

2.5.1.2.2 Drug treatment of amoebiasis

The main members of this group are metronidazole and tinidazole. The other drugs include furazolidone, diloxanide furoate, secnidazole, dehydroemetine, and hydroxy quinolones such as di-iodohydroxyquinoline and iodochlorohydroxyquine. However they are not of much use in practice.

They have wide spectrum of activity covering *Amoeba*, *Trichomonas*, *Giardia lamblia*, bacteria - *Trichomonas* species, *Entamoeba histolytica*, *Giardia lamblia*, anaerobic cocci, gram-negative bacilli, *H. pylori*. They penetrate through the gut by diffusion and gets reduced to intermediate compounds which cause cytotoxicity probably by damaging DNA.

Acute amoebic dysentery

Metronidazole	400 mg t.d.s. for 5 - 10 days, or
Tinidazole	300 mg t.d.s. for 5 - 10 days, plus
Diloxanide furoate	300 - 500 mg t.d.s. for 5 - 10 days

Chronic intestinal amoebiasis

Metronidazole	400 mg t.d.s. for 10 days, or
Tinidazole	300 mg t.d.s. for 5-10 days, or
Secnidazole	1.5 g/day for 5 days single dose, plus
Diloxanide furoate	500 mg t.d.s. for 5-10 days

Hepatic amoebiasis

Metronidazole	400 mg t.d.s. oral for 5 - 10 days, or
Tinidazole	300 mg t.d.s. oral for 10 days, or
Chloroquine	500 mg b.d. for 2 days followed by 250 mg b.d. for 19 days, plus
Diloxanide furoate	500 mg t.d.s. for 5-10 days

Eradication of intestinal infection is to be undertaken with the further course of metronidazole or tinidazole if the cases contain amebic cysts.

In systemic amoebic lesions such as amoebic liver abscess, hepatopulmonary amoebiasis, pleuropulmonary amoebiasis and amoebic brain abscess, i.v. metronidazole 500 mg 8 h for 7-10 days along with broad spectrum antibiotics given orally (tetracycline 250 mg 6 h for 7-10 days or ampicillin 500 mg i.v. 6 h) are undertaken. After instituting systemic chemotherapy, the pus in the liver is aspirated, preferably under ultrasonographic guidance.

Tinidazole is a suitable alternative in those who cannot tolerate metronidazole.

Emetine hydrochloride which used to be given i.m. in a dose of 60 mg daily for 7-10 days both for amoebic dysentery and systemic amoebiasis has been almost totally replaced by metronidazole and tinidazole.

Metronidazole ★

- 1. Amoebiasis, giardiasis, trichomonal vaginitis, anaerobic infections, ulcerative gingivitis, trench mouth, guinea worm infestation, *H. pylori* infection, Vincent's angina, pseudomembranous colitis caused by *C. difficile*, bacteroides fragilis infection.

C/I: Neurological disease, blood dyscrasias, first trimester of pregnancy

Though no teratogenic effect has yet been demonstrated, its mutagenic potential warrants caution.

P/C : Carcinogenicity, pregnancy, breast feeding, adjustment of dosage in old people. Metronidazole may cause dry mouth, contributing to the development of caries, periodontal diseases, oral candidiasis, and discomfort.

S/E : Anorexia, nausea, metallic taste and abdominal cramps, less frequently causes headache, glossitis, dryness of mouth, dizziness, rashes and transient neutropenia. Prolonged administration cause peripheral neuropathy, and CNS effects like seizures have followed very high doses.

P/A : Tablet 200mg, 400 mg, 600 mg.
Suspension 200 mg/5mL.
Injection 500mg/100mL.
Gel 1%

Compound preparations are available with other agents such as diloxonide furoate, nalidixic acid, furazolidone and norfloxacin.

Dose : Amoebiasis: 400 - 800 mg t.d.s. for 5 - 10 days

Trichomoniasis: 2 g single dose / 2 divided doses, or 250 mg t.d.s. for 7 days

Giardiasis: 2 g o.d. for 3 days or 400 mg t.d.s. for 5 days.

Anaerobic infection :15 mg/kg over 1 hour followed by 7.5 mg/kg over 1 hour, 6 h.

Maximum dose 4g/day.

Prophylaxis against post operative infection: 15 mg/kg over 30-60 min before surgery followed by 7.5 mg/kg over 30-60 min 6 and 12 h post operatively.

Bacterial vaginosis : 2 g single dose followed by 500 mg b.d for 7 days

Clostridium difficile colitis : 500 mg t.d.s. for 7 - 10 days along with vancomycin.

H.pylori eradication : 250 mg - 500 mg b.d. or t.d.s. for 1-2 weeks in combination with proton pump inhibitor (omeprazole) and azithromycin.

Pelvic inflammatory disease (PID) : 500 mg b.d. for 14 days along with ofloxacin.

Community acquired pneumonia : 500 mg i.v. or orally, 6 h for 10 days with third generation cephalosporin.

Tetanus : 500 mg 6 h or 1 g b.d. for 10 days.

D/I: Disulfirum like reaction with alcohol, effect of nicoumalone and warfarin enhanced, metronidazole inhibits metabolism of phenytoin (increased plasma - phenytoin concentration), phenobarbitone accelerates metabolism of metronidazole (reduced plasma metronidazole concentration), metronidazole inhibits

2. Anti Infective Agents

metabolism of flurouracil (increased toxicity), increased toxicity reported with lithium. Cimetidine inhibits metabolism (increased plasma metraniazazole concentration).

Cost :	Tab 400mg	(10)	Rs.6.00 - 9.00
		(30g)	Rs.20.00 - 21.00

Tinidazole ♦

I: Nitroimidazole antiprotozoal antibacterial with rapid bacterial action against H Pylori. Effective in infections due to entamoeba histolyca, trichomonas vaginalis, giardia lamblia, anaerobic bacteria.

C/I: Blood dyscrasias, organic neurological diseases, pregnancy, lactation, hypersensitivity.

P/C: Use with caution in alcoholics because of antabuse (disulfiram) like action.

S/E: Hypersensitivity, hypotension, bronchospasm, metallic taste.

P/A: Tablets 300 mg, 500 mg, 600 mg, 1 g, 2 g

Injection 2 mg/mL (400 mL)

Suspension 75 mg/5 mL, 150 mg/5 mL.

Combination tablets with ciprofloxacin, diloxanide furoate, furazolidone, lansoprazole + clarithromycin, omeprazole + amoxycillin are available.

Dose: Amoebiasis : 300 mg t.d.s. for 5-10 days.

Trichomoniasis, giardiasis, bacterial vaginosis : 2 g single dose

Anaerobic infection : 2 g followed by 1 g/day for 5 - 7 days.

Surgical prophylaxis : 2 g 12 h before surgery orally, or 1.6 g single i.v. infusion before surgery.

Peritonitis, abdominal abscess, brain abscess : 800 mg infused as 400 mL solution (2mg/mL) at 10 mL/min followed by 800 mg daily until oral therapy can be given.

D/I: Disulfiram like reaction with alcohol.

Cost:	Tab 500 mg	(4)	Rs. 7.00 - 13.00
	Inj 2mg/mL	(400 mL)	Rs. 40.00 - 50.00
	Susp 150 mg/5 mL	(60 mL)	Rs. 36.00 - 37.00

1.5.2.3 Drugs for Giardiasis

Metronidazole 200 mg t.d.s. for 7 days or 2 g daily for 3 days

Tinidazole 300 mg b.d. for 7 days or 2 g single dose

1.5.2.4 Drugs for Trichomoniasis

Drugs used orally

Metronidazole 200 - 400 mg t d s. for 7 days or 2 g single dose

Tinidazole 300 mg b.d. for 7 days or 2 g single dose

Repeat course can be given after 6 weeks.

Both sex-partners should be treated concurrently.

2. Drugs used intravaginally

Clotrimazole - 100 mg h.s. for 6 - 12 days.

Povidone iodine - 200 mg morning and h.s. for 2 weeks

Flamycin - 2 lac unit/mL suspension applied to the affected area with sterile cotton 2-3 times daily for 7-10 days.

2.6 ANTHELMINTICS

These are drugs used in the treatment of helmenthic infections.

Mebendazole ☆

Broad spectrum anthelmintic.

I: Ascariasis (round worm infestation), ancylostomiasis (hook worm - both species), enterobiasis, trichuriasis, strongyloidiasis.

C/I: In acute surgical abdomen withhold the drug.

P/C: Pregnancy, children less than 2 years, allergic reactions to the drug

S/E: Diarrhoea, nausea, abdominal pain when used in heavy infestation, allergic reactions, alopecia, granulocytopenia.

P/A: Tablet 100 mg, 500 mg

Suspension 100 mg/5 mL (30 mL bottle)

Sachets 200 mg/5 g (5 g sac)

Dose: Round worm, hook worm, trichuris - 100 mg b.d. for 3 consecutive days.

Enterobiasis - 100 mg single dose repeated after 2 - 3 weeks.

D/I: Cimetidine increases plasma mebendazole concentration

Cost:	Tab 100 mg	(6)	Rs 6.00 - 10.00
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Susp	100 mg/5 mL	(30 mL)	Rs. 5.00 - 11.00
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Sac	200 mg/5 g	(5 g)	Rs. 4.00 - 5.00
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Albendazole ☆

Broad spectrum activity, excellent tolerability, single administration is usually effective.

I: Same as that of mebendazole. In addition, it is also effective in hydatid disease, H.nana infestation, strongyloidosis.

C/I: Pregnancy

P/C: Reduced dose in children and prolonged treatment to be avoided

S/E: Gastrointestinal - nausea, vomiting and abdominal pain, dizziness

P/A: Tablet 200 mg, 400 mg

Suspension 200 mg/5 mL (10 mL, 50 mL bottle)

2. Anti Infective Agents

Dose Round worm, hook worm, trichuris trichiura - single dose 400 mg for adults to be chewed.

Enterobiasis : 200 mg for children below 8 years.

Tape worms, strongyloidosis - 400 mg daily for 3 consecutive days

Neurocysticercosis - 15 mg/kg/day for 1 months or more

Hydatid disease - 400 mg b.d. for 4 weeks, repeat after 2 weeks if needed.

D/I: No significant interactions.

Cost :	Tab	400 mg	(2)	Rs. 7.00 - 12.00
	Susp	200 mg/ 5 mL :	(10 mL)	Rs. 10.00 - 15.00

Pyrantel pamoate ✱

I: Ascariasis, enterobiasis, ancylostomiasis

C/I: Pregnancy, children and those with impaired liver function.

P/C: To be given with care in pregnant women and children below 2 years.

S/E: GI side effects, headache and dizziness.

P/A: Tablet 200 mg, 250 mg.

Suspension 200 and 250 mg/5 mL (8 mL and 10 mL bottle), 25 and 50 mg/mL (8 mL and 10 mL bottle)

Dose : Single dose 10 - 15 mg/kg

D/I: Anthelmintic action of pamoate antagonised by piperazine.

Cost :	Tab	250 mg	(3)	Rs. 7.00 - 12.00
	Susp	250 mg/5 mL	(10 mL)	Rs. 8.00 - 12.00

Piperazine

I: Highly active against ascaris and enterobius, can be used in pregnancy.

C/I: Renal insufficiency, hepatic failure, epilepsy.

P/C: Use with caution in the above conditions.

S/E: Safe and well tolerated. Occasionally nausea, vomiting, abdominal discomfort, urticaria, dizziness, excitement and convulsions in toxic doses.

P/A: Tablet 500 mg

Syrup 750 mg/5 mL (30, 115 and 455 mL bottle)

Dose : Round worm : 75 mg / kg (maximum 3.5 mg) single daily dose for 2 consecutive days.

Enterobiasis - 50 mg/kg o.d. for 7 days.

D/I: Antagonises anthelmintic action of pyrantel pamoate

Cost :	Tab	500 mg	(8)	Rs. 4.00 - 5.00
	Syrup	750 mg/5 mL	(30 mL)	Rs. 7.00 - 9.00

Levamisole

I: Ascariasis infestation, ancylostomiasis

- C/I: Blood dyscrasias, renal disease, psoriatic arthropathy, hypersensitivity.
- P/C: Use with care in alcoholics since it produce antabuse-like reaction.
- S/E: Nausea, abdominal pain, giddiness, drowsiness, insomnia.
- P/A: Tablet 50 mg and 150 mg.
Capsules 150 mg.
Syrup 15 mg/5 mL (10 mL bottle)
Suspension 40 mg/5 mL (10 mL bottle)
- Dose: Ascariasis infestation : single doses
Ancylostomiasis : 2 dose at 12 hrs interval
Children < 40 kg: 50 mg
Adult: 150 mg.
- D/I: Increases the serum concentration of phenytoin, potentiates oral anticoagulants.
- Cost : Tab 50 mg (1) Rs. 3.00 - 4.00
Caps 150 mg (1) Rs. 3.00 - 4.00
Syrup 50 mg/5 mL (10 mL) Rs. 4.00 - 6.00
Susp 40 mg/5 mL (10) Rs. 3.00 - 4.00

Thiabendazole

This was the first anthelmintic introduced for the treatment of multiple worm infestation. It is not widely used because of nonavailability.

Diethylcarbamazine citrate ★

- I: Effective drug available for filariasis caused by *W.bancrofti*, *B.malayi*, *Loa loa*, *O.volvulus* and tropical eosinophilia
- C/I: Pregnancy, hypersensitivity.
- P/C: The first dose should be given with caution since intense allergic reactions may follow.
- S/E: Nausea, loss of appetite, headache, dizziness, febrile reaction with rash, pruritus, and enlargement of lymphnodes.
- P/A: Tablets 50, 100 and 150 mg.
Syrup 50 mg/5 mL (60 mL bottle), 120 mg/5 mL (100 and 114 mL bottle)
- Dose : Filariasis : 6-12 mg/kg t.d.s. for 10 - 20 days
Loa Loa : 2 mg/kg for 3 - 4 weeks.
- D/I: No significant interactions
- Cost: Tab 100 mg (10) Rs. 3.00 - 4.00
Syrup 50 mg / 5 mL (60 mL) Rs. 8.00 - 9.00

Ivermectin

- I: Very effective in onchocerciasis and filariasis.

- C/I: Pregnancy.
P/C: Use with caution in children < 5 years, allergic reactions
S/E: Mild itching, postural hypotension, dizziness, transient ECG changes.
P/A: Not freely available. Available only under special circumstances.
Dose: 0.15 - 0.2 mg/kg orally.
D/I: None reported.
Cost: Not freely available.

Niclosamide ✧

- I: *T. saginata*, *T. solium*, *D. latum*, *H. nana* and *D. caninum* infestation.
C/I: Hypersensitivity
P/C: Relatively safe.
S/E: Tremor, abdominal symptoms, pruritus, light headedness.
P/A: Tablet 500 mg
Dose: 2 tablets of 0.5 mg after light breakfast followed by another 2 tablets after 1 hour. A saline purge after 2 hours of last dose. Tablets must be thoroughly chewed before swallowing and washed down with minimum quantity of water.
D/I: None reported
Cost: Tab 500 mg (4) Rs. 22.00 - 23.00

Niridazole

- I: Drug of choice for guinea worm infestation
C/I: Epilepsy, severe heart disease.
P/C: Caution in impaired liver damage and G6PD deficiency.
S/E: Cardio vascular and central nervous system related.
P/A: Not commercially available.
Dose: 25 mg/kg/day (Maximum 1.5 g/day) for 10 days.
D/I: None reported.

Praziquantel ✧

- I: Tape worms, neurocysticercosis and cysticercosis in other parts of the body, schistosomes, other flukes.
C/I: Ocular cysticercosis, lactation, pregnancy.
P/C: Avoid automobile driving or operating heavy machinery for 24 hrs after last dose.
S/E: Dizziness, drowsiness, headache, vomiting, allergy. When given for neurocysticercosis it may cause hyperthermia, seizure and intracranial hypertension.
P/A: Tablet 500 mg, 600mg.

Dose : Tape worms

T.saginata, *T.solium*: 10 mg/kg, single dose morning

H.nana *D.latum*: 15 - 25 mg/kg, single dose morning

Neurocysticercosis: 50 mg/kg daily in 3 divided doses for 15 days.

Corticosteroids should be started along with praziquantel to prevent cerebral oedema.

Schistosomiasis: 40 - 75 mg/kg single dose.

D/I: Carbamazepine and phenytoin decreases praziquantel bioavailability, cimetidine increases praziquantel bioavailability.

Cost: Tab 600 mg (8) Rs. 330.00 - 335.00

2.6.1 CHOICE OF DRUGS FOR HELMENTHIASIS

Worm	First choice of Drugs	Alternatives
Round worm	Mebendazole Albendazole Pyrantel pamoate	Piperazine Levamisole
Hook worm	Pyrantel pamoate Mebendazole Albendazole	Levamisole
Thread worm	Mebendazole	Piperazine
Strongyloides- stercoralis	Thiabendazole	Mebendazole
Whip worm Albendazole	Mebendazole	-----
Trichinella spiralis	Thiabendazole	Mebendazole
Filaria	Diethyl carbamazine	Ivermectin
Tape worms	Niclosamide Praziquantel	Mebendazole Albendazole
Hydatid Diseases	Albendazole Mebendazole	-----
Guinea Worm	Niridazole Metronidazole	-----

Topical NSAIDs may provide some slight relief of pain in musculoskeletal conditions. These should be applied with gentle massage. Avoid contact with eyes, mucous membrane and inflamed and broken skin. Discontinue if rashes develop. They are not to be used with occlusive dressings. Not generally suitable for children.

CHAPTER 3 : DRUGS USED IN GASTROINTESTINAL DISORDERS

3.1 ANTACIDS

Aluminium hydroxide ✧

Magnesium carbonate

Calcium carbonate ✧

Magnesium hydroxide ✧

Magnesium trisilicate

Sodium bicarbonate

Antacids neutralizes gastric hydrochloric acid by forming chlorides, water and carbon dioxide.

I: Peptic ulcer, gastro-oesophageal reflux, neutralization of gastric acid to protect from aspiration pneumonitis during anaesthesia, preparation of endoscopy, prophylaxis of stress ulceration.

C/I: Renal insufficiency, heart failure, hypertension, young children.

P/C: Antacids are considered safe as long as high doses are avoided on a long term basis.

Antacids should not be given to young children (up to 6 years of age) unless specifically indicated.

S/E: Aluminium salts: constipation, phosphate depletion, muscle weakness, and osteoporosis.

Magnesium salts: diarrhoea.

Calcium salts: hypercalcemia, nephrolithiasis, acid rebound hyperacidity.

Sodium salts: sodium overload, systemic alkalosis.

P/A: Only combinations are available.

Chewable tablets, gel

Dose: Aluminium hydroxide: Tabs : 0.5-1 g q.d.s.

Magnesium hydroxide: 5 mL as milk of magnesia q.d.s.

Magnesium carbonate: 0.5-1g q.d.s.

Magnesium trisilicate: 1-2 g q.d.s.

Calcium carbonate: 2-4 g

Sodium bicarbonate: 1-5 g

D/I: Antacids impair the absorption of several drugs and thereby their effects are reduced. Most interaction can be avoided by taking antacids 2 hrs before or after ingestion of other drugs. The bioavailability of iron, theophylline, quinolones, tetracycline, INH, ketoconazole, ethambutol, benzodiazepines, phenothiazines, ranitidine, phenytoin, indomethacin, nitrofurantoin, fluoride, phosphate, prednisone, procainamide, atenolol and propranolol.

Rate of elimination for salicylates and phenobarbital are increased. In the case of amphetamine, ephedrine, mecamlamine, pseudoephedrine and quinine rate of elimination is reduced.

Note: No single antacid is satisfactory for all circumstances and therefore mixtures are often used.

eg. Sodium bicarbonate for quickest effect supplemented by magnesium hydroxide or magnesium carbonate. Disturbed bowel habits may be altered by altering the proportion of magnesium salts and aluminium salts.

Tablets are more convenient, but act more slowly unless chewed or sucked. A liquid preparation may be more acceptable for frequent use. An antacid taken in an empty stomach is effective only for 20 - 40 min because of gastric emptying. When it is taken an hour after a meal, the effect may last for 2 - 3 hrs.

Cost: Only combinations of more than one drug are available.

Tab 10 Rs. 2.00 - 6.00

Gel 200 mL Rs. 14.00 - 20.00

3.2 ULCER HEALING DRUGS

3.2.1 H_2 Receptor Antagonists

Cimetidine

Inhibits gastric acid secretion by its H_2 receptor blocking action. It was the first H_2 receptor blocker introduced in therapeutics with the advent of different H_2 receptor blockers to proton pump inhibitor, cimetidine.

I: Duodenal ulcer, gastric ulcer, stress ulcers and gastritis, reflux oesophagitis, Zollinger-Ellison syndrome, prophylaxis of aspiration pneumonia during anaesthesia and surgery.

C/I: Hypersensitivity.

P/C: Impaired renal and hepatic function, pregnancy and lactation, gastric malignancy.

S/E: CNS disturbances, gynecomastia, blood dyscrasias.

P/A: Tablet 200 mg, 400 mg.

Injection 200 mg/mL

Dose: Oral: 400 mg o.d. to q.d.s. depending on the indication.
Maximum 2400 mg/day.

i.m.: 300 mg t.d.s. or q.d.s.

i.v.: Diluted 300 mg to 20 mL with normal saline and inject over not less than 2 minutes.

D/I: Absorption reduced by antacids. May potentiate antacids, anticoagulants, phenytoin, theophylline, benzodiazepines, beta blockers, lignocaine.

Note: Not much use in clinical practice.

Cost: Tab 200 mg (10) Rs. 7.00 - 18.00

Inj 200 mg/mL (2 mL) Rs. 3.50

3. Drugs used in Gastrointestinal Disorders

Ranitidine ☆

In general the H_2 receptor antagonists and proton pump inhibitors are given in full doses for 4-6 weeks and thereafter at a lower doses for 1 or 2 months by which time ulcer would have healed. Cigarette smoking, alcoholism and irregular timing of food are the common causes for relapse of the ulcer. These should be avoided.

I: Same as cimetidine.

C/I: Known hypersensitivity to the drug.

P/C: Impaired renal function, pregnancy and lactation, not recommended for children below 8 years.

Exclude gastric malignancy before starting treatment. It may cause headache, dizziness and rarely hepatitis and thrombocytopenia.

S/E: Blurred vision, allergic reaction, loss of hair, antiandrogenic effect.

P/A: Tablets 150 mg, 300 mg

Injection 50 mg / 2 mL

Dose: For ulcer healing: 150 mg b.d. or 300 mg at h.s. for 4 - 5 weeks

Maintenance: 150 mg at h.s. for 6 months to 1 year.

Zollinger-Ellison syndrome: 150 mg t.d.s. to a maximum of 900 mg/day in divided doses.

Parenteral: i.m. 50 mg 6 to 8 h.

i.v. 2 mL ampoule to 20 mL with Normal saline and inject over ≥ 5 minutes every 6 to 8 h.

D/I: It does not significantly inhibit hepatic metabolism of other drugs.

Cost: Tab 150 mg (10) Rs. 10.00-16.00

Inj 50 mg/2mL (2mL) Rs. 3.00

Famotidine

I, C/I, D/I: Same as ranitidine.

P/C: Impaired renal function, pregnancy and lactation, not recommended in children. It may cause headache, rashes and dizziness.

S/E: Confusion, antiandrogenic effect, dryness of mouth and skin, skin rashes.

P/A: Tablet 20 mg, 40 mg

Injection 20 mg/mL

Dose: Benign gastric and duodenal ulceration - 40 mg orally at h.s. for 4 - 8 weeks

Maintenance - 20 mg orally at h.s.

Zollinger-Ellison syndrome: 20 mg every 6 h.

Parenteral: 20 mg i.v. every 12 h. after dilution to 5 - 10 mL with a compatible i.v. solution.

Cost: Tab 20mg (10) Rs. 4.00-18.00

Inj 20mg/mL (2mL) Rs. 3.00

Nizatidine

I:; C/I:; D/I: : Same as ranitidine

P/C: Laboratory value alterations - increases serum aspartate aminotransferase concentrations. May cause false positive reaction with urine urobilinogen test.

S/E: Increase in sweating, antiandrogenic effect, head ache, skin rash, nausea and vomiting.

P/A: Tablet 150 mg and 300 mg.

Injection 25 mg / mL for dilution and use as i.v. infusion.

Dose: Duodenal / gastric ulcer : 150 mg b.d. or 300 mg in the evening for 4 - 8 weeks.

Maintenance : 150 mg at night.

Cost : Not freely available.

Roxatidine

I:; C/I:; D/I: : Same as ranitidine

P/C: Impaired renal function, pregnancy and lactation. Not recommended in children less than 14 years. Should not be used in patient with malignant gastric ulcer.

S/E: Occasional headache, GI disturbances, sleep disturbances, restlessness.

P/A: Tablet 75 mg,

Sustained release tablet 75mg, 150 mg.

Dose: For ulcer healing 75 mg tablet b.d. or 150 mg sustained release tablet at h.s. for 4 - 6 weeks.

Maintenance : 75 mg at h.s.

D/I: No interaction with other drugs. Concomitant intake of food or antacids has no effect on its pharmacokinetics.

Cost : SR Tab 75mg (14) Rs.40.00

3.2.2 Proton Pump Inhibitors

These agents inhibit gastric acid by blocking the hydrogen potassium - ATPase enzyme system in gastric parietal cells. The enzyme inhibited is thought to be necessary for the terminal step in gastric acid production. So both basal and stimulated acid secretion are reduced.

Omeprazole

I: Promote healing of ulcers in the stomach, duodenum and oesophagus. Patients who do not respond adequately of H_2 receptor antagonists, Zollinger - Ellison syndrome.

C/I: Pregnancy and lactation.

P/C: Exclude gastric malignancy before and during treatment.

3. Drugs used in Gastrointestinal Disorders

S/E : Haematological abnormalities, specifically anaemia, haematuria, urinary tract infections, nausea, occasional headache, diarrhoea, constipation, flatulence and rashes.

P/A : Capsule 10 mg and 20 mg.

Dose : Reflux oesophagitis : 40 mg daily for 8 weeks

Duodenal ulcer : 20 mg daily for 4 weeks.

Gastric ulcer : 20 mg daily for 8 weeks.

D/I : Omeprazole reduce the metabolism of diazepam, phenytoin and R-isomer of warfarin.

Cost : Cap 10 mg (10) Rs. 17.00 - 20.00

Cap 20 mg (10) Rs. 38.00 - 100.00

Lansoprazole

I: Duodenal and benign gastric ulcer, gastro oesophageal reflux disease, particular value in patients who do not respond to H_2 receptor antagonists, Zollinger - Ellison syndrome. Lansoprazole has been shown to be more effective in patients with reflux oesophagitis.

C/I, P/C, S/E, D/I: Similar to omeprazole.

P/A : Capsule 15 mg, 30 mg.

Dose : 15 - 30 mg daily.

Duodenal ulcer : 30 mg daily for 4 weeks.

Gastric ulcer : 30 mg daily.

Gastro oesophageal reflux disease(GORD) - 30 mg daily for 4 - 8 weeks.

D/I: Decrease the metabolism of phenytoin, diazepam and R-isomer of warfarin.

Cost: Cap 15 mg (10) Rs 25.00-28.00

In the ordinary case ulcer healing occurs in about 4-6 weeks. There after reduced maintenance dose may be used for about one month except in Zollinger - Ellison syndrome and recurrent ulcers.

3.2.3 Drugs against Helicobacter Pylori (H.Pylori)

Eradication of H.Pylori is a very important component of curative therapy of peptic ulcer and other diseases associated with H.pylori. Persistence of H.Pylori predisposes to relapse.

Triple therapy : This regimen is currently recommended for the eradication of H.pylori. In 90% of cases eradication can be achieved.

1. Metronidazole - 250 mg t.d.s. +

2. A bismuth compound (bismuth subsalicylate - 2 tablets q.d.s. or colloidal bismuth subcitrate - 120 mg q.d.s.) +

3. Tetracycline - 500 mg q.d.s. or amoxycillin - 500 mg t.d.s.

All three drugs to be given for 2 weeks in treating peptic ulcer. Therapeutic limitations of triple drug therapy are compliance, cost and side effects (nausea, diarrhoea, dizziness)

Alternate combination therapy which is quite effective consists of omeprazole 20 mg b.d. + clarithromycin 500 mg b.d. + tinidazole 300mg b.d. all given for 2 weeks

Note: Amoxycillin 500mg b.d. may be given instead of clarithromycin and metronidazole 400mg b.d. may be used instead of tinidazole.

Bismuth compounds

Mechanism of action

Cytoprotection by

- Enhanced secretion of mucus and bicarbonate
 - Inhibition of pepsin activity.
 - Accumulation of bismuth subcitrate preferentially in the craters of gastric ulcer, (Complex bismuth salts of citric acid at acid pH chelates with protein in the ulcer base and may form a protective barrier against acid diffusion and peptic digestion)
- I: Antibacterial action against *H.pylori*, healing of both gastric and duodenal ulcers as effectively as cimetidine, prevention of ulcer recurrence, and traveller's diarrhoea.

C/I: Bleeding ulcers or haemorrhagic states, dehydration, acute dysentery, haemophilia.

P/C: Bismuth reacts with bacterial hydrogen sulfide and forms bismuth sulfide which imparts a black colour to the oral cavity and faeces, toxicity to bismuth causes ataxia, encephalopathy and osteodystrophy.

S/E: Bismuth encephalopathy, severe constipation.

Dose: Colloid bismuth subcitrate : 120 mg orally q.d.s.

Bismuth subsalicylate : 2 tabs orally q.d.s.

D/I: Patients taking large quantities of aspirin or with sensitivity to aspirin also show cross sensitivity to salicylate moiety in bismuth salicylate. It reduces bioavailability of orally administered tetracycline.

Cost: Not freely available.

Metronidazole ☆

I: *H.pylori* infection.

Dose: *H.pylori* eradication : 250 mg - 500 mg b.d or t.d.s for 1-2 weeks in combination with proton pump inhibitor (omeprazole) and azithromycin.

3. Drugs used in Gastrointestinal Disorders

Tinidazole

Dose: 300mg b.d. or t.d.s. for 5-7 days
Parenteral: 300mg b.d. 3-5 days i.v.

Clarithromycin

It has bactericidal activity against H.pylori.

- I: Upper and lower respiratory tract infections, skin and soft tissue infections, eradication of H.Pylori along with acid suppression.

Dose: Oral 250 to 500 mg b.d. for 7 - 14 days.

3.3 ANTISPASMODICS

Dicyclomine ✧

It blocks the muscarinic actions of acetylcholine by competing with acetylcholine for the muscarinic receptors.

- I: Intestinal colic, ureteric colic, biliary colic, dysmenorrhoea.

C/I: Intestinal obstruction, urinary retention, glaucoma, infants below 6 months, reflux oesophagitis, liver disease, renal disease, pregnancy and lactation.

P/C: Can cause respiratory arrest in infants below 1 month, exacerbation of glaucoma, exacerbation of acute urinary retention.

S/E: Dry mouth with difficulty in swallowing and thirst, dilatation of the pupils with loss of accommodation and sensitivity to light, increased intra ocular pressure, flushing, dry skin, bradycardia followed by tachycardia, palpitations and arrhythmias, difficulty in micturition, constipation; rarely fever, confusional states and rashes.

P/A: Tablet 20 mg

Injection 10mg/mL, 20mg/2mL

Drops 100 mg/mL

Dose: Oral: 10 - 20 mg t.d.s.

Parenteral route

Adults: 20 mg i.m. 8 h

Children: 10 mg i.m. 8 h

D/I: No significant interactions

Cost: Tab 20 mg (10) Rs. 4.00 - 8.00

Inj 10mg/mL (2mL) Rs. 4.00

Drops 100mg/mL (10mL) Rs. 11.00

Hyoscine butyl bromide ✧

- I: Intestinal, biliary and ureteric colics, spasmodic dysmenorrhoea, preparatory regimen for special radiological investigations such as hypotonic duodenography and for GI endoscopy.

- C/I: Intestinal obstruction, glaucoma, hepatic or renal failure, pregnancy and lactation.
- P/C: Avoid driving or operating machinery.
- S/E: Dry mouth, thirst, increased intraocular pressure, flushing, palpitations followed by arrhythmias, constipation and difficulty in micturition, rashes.
- P/A: Tablets 10mg
Injection 20mg/mL
- Dose: Oral: 10 mg t.d.s.
Parenteral route: 10 - 20 mg i.m. or i.v. 8 h.
- D/I: Other anticholinergic drugs and tricyclic antidepressants and alcohol potentiates the effects of hyoscine butyl bromide.
- Cost: Tab 10mg (10) Rs.15.00 - 17.00
Inj 20mg/mL (1mL) Rs. 5.00

Atropine sulphate

Dose: 0.6 mg i.m.

3.4 ANTIEMETICS AND PROKINETICS

Metoclopramide ☆

It is a dopamine - D₂ receptor antagonist

- I: Nausea and vomiting associated with GI disorders, post surgical conditions such as postoperative gastric stasis and regurgitation, treatment with cytotoxics and radiotherapy in cancer patients. As a prokinetic agent in vague gaseous dyspepsias and reflux oesophagitis.
- C/I: Carcinoma breast, phaeochromocytoma, extrapyramidal disease, mechanical obstruction of GI tract.
- P/C: Hepatic and renal impairment, pregnancy and lactation. For the elderly and children reduce the dose
- S/E: Note: Methemoglobinemia has been reported in premature and full term neonates receiving metoclopramide i.m. at a dose of 1-2 mg/kg bw/day for 3 days or more.
Agranulocytosis, cardio vascular effects such as hypotension, hypertension or tachycardia. Extrapyramidal symptoms such as parkinsonism and tardive dyskinesia may occur. High doses lead to agitation, panic like states and restless legs syndrome. If tardive dyskinesia occur, i.m. injection of promethazine in a dose of 0.5 mg/kg bw will alleviate the symptoms.
- P/A: Tablet 10 mg, 15mg,
Injection 5mg/mL,

3. Drugs used in Gastrointestinal Disorders

Syrup 5mg/5mL,

Liquid 5mg/5mL.

Dose: Oral: 0.5 mg/kg bw/dose

5-10 mg t.d.s. or 10-20 mg i.v.

Parenteral:

Post operative nausea: i.m -10 mg at the end of surgery
i.v.-1-2 mg/kg/dose 15-30 min
before beginning cancer
chemotherapy.

Cost:	Tab	10mg	(10)	Rs.4.00-8.00
	Inj	5mg/mL	(2mL)	Rs.4.00
	Syrup	5mg/5mL	(30mL)	Rs.6.00-11.00
	Liquid	5mg/5mL	(30mL)	Rs.11.00-14.00

Isopropamide

It is a synthetic anticholinergic drug, antisecretory.

I: Gastritis, acid-peptic disease (APD), GI disorders caused by or complicated by mental or emotional factors.

C/I: Glaucoma, hepatic impairment, pyloric stenosis, prostatic enlargement.

P/C: Cardiovascular disease, pregnancy and lactation, children and elderly.

S/E: Dry mouth, tachycardia, palpitation, constipation, insomnia, blurred vision, restlessness.

P/A: Only combinations are available

Tablets (isopropamide 5mg + trifluoperazine Hcl 1mg)

Dose: 5 mg b.d.

D/I: Additive effect with amantidine, phenothiazines and tricyclic antidepressants. This drug reduces gastric motility and hence the absorption of other drugs.

Cost: Tab (isopropamide 5mg, trifluoperazine Hcl 1mg) (10) Rs.5.00

Domperidone ♦

This is dopamine D_2 receptor antagonist. It acts centrally in chemoreceptor trigger zone (CTZ) and peripherally in upper GIT. Increases gastro oesophageal sphincter pressure and gastric emptying.

I: Nausea and vomiting associated with gastrointestinal disorders, functional dyspepsia, and motility disorders such as hypomotility, irritable bowel syndrome and others. It is used as an antiemetic in cancer chemotherapy.

C/I: Pregnancy.

P/C: Reduce the dose in children.

S/E: Raised prolactin concentrations possibly leading to galactorrhoea and gynecomastia, acute dystonic reactions.

P/A: Tablets 5mg, 10mg,
Syrup 1mg/mL,
Suspension 1mg/mL,
Drops 10 mg/mL

Dose: 10 - 20 mg t.d.s. or q.d.s. (adults)

Children : 0.3 mg/kg t.d.s or q.d.s.

D/I: Opioid analgesics and antimuscarinics cause antagonism of the effect on GI activity.

Cost:	Tab	10mg	(10)	Rs.14.00-20.00
	Syrup	1mg/mL	(30mL)	Rs.20.00
	Suspension	1mg/mL	(30mL)	Rs.15.00-20.00
	Drop	10 mg/mL	(5 mL)	Rs. 14.00 - 15.00

Cisapride

Increases motility throughout the GIT by enhancing acetylcholine availability in the gut wall.

I: To relieve symptoms of gastroesophageal reflux disease, reflux oesophagitis, dyspepsia, impaired gastric emptying secondary to diabetes, systemic sclerosis etc.

C/I: Pregnancy, conditions where GI stimulation is dangerous such as in GI haemorrhage, and mechanical obstruction.

P/C: Reduce the dose by half in hepatic and renal insufficiency and in the elderly.

S/E: Abdominal cramps; constipation; diarrhoea which is dose-related, fatigue, headache, nausea and somnolence.

P/A: Tablets 5mg, 10mg, 20mg,
Suspension 1mg/mL

Dose: 10 mg t.d.s. x 4 - 6 weeks.

D/I: Opioid anagesics and antimuscarinics antagonise the effect on GI motility. Cisapride enhances the effects of oral anticoagulants.

Cost:	Tab	10mg	(10)	Rs.23.00-38.00
	Susp	1mg/mL	(30mL)	Rs.19.00

Clidinium

I: Irritable bowel syndrome, nervous dyspepsia.

C/I: Hypersensitivity, glaucoma, bladder neck obstruction, GI obstruction, pregnancy.

3. Drugs used in Gastrointestinal Disorders

- P/C:** Hepatic and renal impairment, elderly, lactating mothers, hypertension.
- S/E:** Blurred vision, dry mouth, constipation, muscle weakness, drowsiness. Avoid driving automobiles while on this drug
- P/A:** Only combinations are available.
Tablets (clidinium bromide 2.5mg, chlordiazepoxide 5mg)
- Dose:** 2.5 - 5 mg daily before meals and at h.s.
- D/I:** Additive anticholinergic effects with antidepressants, quinidine, and some of the antihistamines.
- Cost:** Tab (clidinium bromide 2.5mg, chlordiazepoxide 5mg) (10) Rs.8.00-10.00
Tab (clidinium bromide 2.5mg, chlordiazepoxide, dicyclomin Hcl 10 mg) (10) Rs.9.00-10.00

Mebeverine

This is an antispasmodic which has direct effect on colonic muscle activity.

- I:** Irritable bowel syndrome, organic bowel diseases.
- C/I:** Hypersensitivity, lactation, children below 2 years, neonates
- P/C:** Hepatic and renal impairment, severe ischaemic heart disease, pregnancy.
- S/E:** Vague dyspepsia, heartburn, dizziness.
- P/A:** Tablets 135mg
- Dose:** 135 mg t.d.s. 20 min before meals.
- D/I:** None
- Cost:** Tab 135mg (10) Rs.79.00

Ondansetron

Selective 5- HT₃ receptor antagonist. Peripheral action on vagal nerve terminals and centrally in CTZ.

- I:** Nausea and vomiting associated with cancer chemotherapy and radiotherapy, post operative nausea and vomiting.
- C/I:** Hypersensitivity, lactation.
- P/C:** Hepatic impairment, elderly, pregnancy
- S/E:** Note : Since ondansetron is used in conjunction with cancer chemotherapeutic agents, it is difficult to attribute some side effects, such as diarrhoea and fever, to ondansetron alone. Rarely anaphylaxis, bronchospasm and chest pain may occur. Constipation, diarrhoea, fever, headache are more frequent.
- P/A:** Tablets 4mg, 8mg,
Injection 2mg/mL 2mL, 4mL.

Dose : 8 mg slow i.v. give 30-45 min before chemotherapy / radiotherapy or 8 mg orally 1 - 2 h before chemo/ radiotherapy followed by 8 mg orally 12 h.

D/I: Dexamthasone potentiates the effect of the drug.

Cost: Tab 4mg (10) Rs.75.00-80.00

Inj 2mg/mL (2mL) Rs.20.00-25.00

Nabilone

This is a synthetic cannabinoid antiemetic

I: Nausea and vomiting caused by cytotoxic chemotherapy unresponsive to conventional antiemetics.

C/I: Severe hepatic impairment.

P/C: Elderly, hypertensive heart disease, history of psychiatric disorder.

S/E: Psychiatric effects, difficulty in breathing, hypotension, increase in blood pressure, difficulty in concentrating, dizziness.

P/A: Capsules. 1 mg.

Dose : 1 - 2 mg b.d.

D/I: Alcohol, anxiolytics and hypnotics enhance the sedative effect of nabilone.

Cost : Not freely available.

Prochlorperazine ☆

Phenothiazine group. Action is mainly by dopamine receptor antagonism.

I: Nausea and vomiting associated with labyrinthine disorders, migraine, Meniere's disease.

C/I: Hypersensitivity, CNS depression, coma, bone marrow depression.

P/C: Extrapyrimal syndromes, hepatic impairment, epilepsy, pregnancy, lactation, children under 2 years, glaucoma.

S/E: Severe dystonic reactions some times occur, especially in children, elderly and debilitated.

P/A: Tablets 5mg, 25mg,

Injection 12.5mg/mL 1mL.

Dose : Adults : 5 - 10 mg b.d. or t.d.s.

Children : 0.25 mg/kg/bw b.d. or t.d.s..

D/I: Potentiates other CNS depressants like alcohol, hypnotics, sedatives, barbiturates, opioids and general anaesthetics. Additive anticholinergic effect with antihistamines, tricyclic antidepressants and antiparkinsonian drugs.

Cost: Tab 5mg (10) Rs.8.00

Inj 12.5mg/mL (10 x 1mL) Rs.41.00

3. Drugs used in Gastrointestinal Disorders

Promethazine

It is an antiemetic phenothiazine group of drug with sedative effects

Dose: oral : 25 mg b.d.

parenteral : 0.5 mg /kg bw i.m., or i.v. for quicker action.

3.5 ANTIDIARRHOEALS

Diarrhoea is a symptom of several different types of pathological processes affecting different parts of the alimentary tract. eg. enteritis and malabsorption affecting the small intestine; colitis affecting the large intestine; irritable bowel syndrome affecting several parts of the GIT and pancreatic cholera which is due to extra alimentary causes. The other common causes include adverse side effects of drugs, anxiety and thyrotoxicosis. Therefore the symptomatic treatment of diarrhoea by antidiarrhoeal drugs is to be decided on individual merits. In case of infective diarrhoea such as gastroenteritis and dysenteries, treatment of the primary condition arrests the diarrhoea usually. In infective diarrhoea and malabsorption states primary antidiarrhoeal agents are generally contraindicated. Specific antidiarrhoeal agents are indicated in special situations as adjuvant to primary therapy or in conditions where no other primary removable causes are detectable.

Loperamide ✧

Opioid antidiarrhoeal. Reduces motility by its direct action on intestinal smooth muscle.

I: Acute nonspecific diarrhoea, chronic diarrhoea in adults.

C/I: Severe diarrhoea where inhibition of peristalsis is not desirable, acute pseudomembranous enterocolitis and children < 4 years.

P/C: Children upto 6 years, in geriatric patients.

S/E: Allergic reaction, toxic megacolon, bloating, loss of appetite, severe abdominal pain with nausea and vomiting, dizziness, dryness of mouth.

P/A: Tablets 2mg,

Capsules 2 mg,

Liquid 1mg/5mL.

Dose: 2 - 4 mg repeated after each loose motion, not to exceed 16 mg/day.

D/I: None reported.

Cost :	Tab	2mg	(10)	Rs.5.00-8.00
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	Liquid	1mg/5mL	(30 mL)	Rs.9.00
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Codeine phosphate ✧

Opioid antidiarrhoeal. Reduces intestinal motility by its direct action on intestinal smooth muscle. It also has antisecretory effect.

I: Acute non specific diarrhoeas, chronic diarrhoea in adults.

C/I: Liver disease, ventilatory failure.

P/C: Hypotension, hypothyroidism, asthma, decreased respiratory reserve, prostatic hypertrophy, pregnancy and breast feeding, hepatic impairment; renal impairment, and opioid dependence. Severe withdrawal symptoms if the opioids are withdrawn abruptly.

S/E: Nausea and vomiting, constipation and drowsiness, larger doses produce respiratory depression and hypotension; difficulty in micturition, ureteric and biliary spasm, dry mouth, sweating, headache, facial flushing, vertigo, bradycardia, palpitation, postural hypotension, hypothermia, hallucinations, miosis, decreased libido or potency, rashes, pruritus and dependence.

P/A: Syrup 15mg/5mL

Tablet 15mg

Dose: 15 - 60 mg at 8 h intervals.

D/I: Alcohol, anxiolytics and sedatives enhance the sedative effect.

Cost:	Syrup	15mg/5mL	(100mL)	Rs.23.00
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	Tab	15mg	(10)	Rs.10.00
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Diphenoxylate

I, C/I, P/C, S/E, D/I: - Same as codeine phosphate.

P/A: Only combinations are available

Tablet containing diphenoxylate hydrochloride 2.5mg, and atropine sulphate 0.025mg)

Dose: 5 mg 3 - 4 t.d.s. or q.d.s./ day

Cost: Tab (diphenoxylate hydrochloride 2.5mg and atropine sulphate 0.025mg) (10) Rs.3.00

Lactobacillus Acidophilus

This is not a primary antidiarrhoeal agent. In conditions where the intestinal flora have been deranged as a result of antibiotic and other forms of therapy, it can be used as an adjunct to restore intestinal microbial flora and give symptomatic relief. Promotes the growth of saccharolytic flora and alter the intestinal pH so as to inhibit the growth of pathogens.

I: Used in the treatment of certain chronic diarrhoea.

P/A: Only combinations are available

Dispersible tablets, capsules, sachets.

Dose: 1 Capsule per day.

1 sachet b.d.

Cost: Disp tab (lactobacilli sporogenes 40 x10 lakhs, (10nos) Rs 11 00

3. Drugs used in Gastrointestinal Disorders

	vit.B ₁ 2mg, B ₂ 2.5mg, B ₆ 1.5mg, nicotinamide 20 mg)	
Cap	(lactobacillus acidophilus 1000 lacs, (10nos) vit.B ₁ 10mg, B ₂ 10mg, B ₆ 3mg, B ₁₂ 15 mcg, folic acid 1500 mcg, niacinamide 100 mg, calcium pantothenate 20 mg, vit c 75mg.)	Rs 17.00
Sachets	(Lactic acid bacillus 150 million spores/1.8 g powder) (20 nos)	Rs 50.00

3.6 LAXATIVES

These drugs are employed to relieve constipation. They act in several ways -softening the faecal matter, increasing its bulk and improving intestinal motility. They are drugs which are widely sold over the counters and hence greatly misused, especially by the elders. Absolute medical indications for laxatives are only limited. These include symptomatic discomfort due to constipation occurring as the result of recumbency, febrile states, dehydration or any other causes where correction of the primary cause takes time.

- I: Symptomatic constipation, discomfort and anxiety due to prolonged constipation. Clearance of the loaded colon prior to contrast radiography, endoscopic procedures. In hepatic failure where bacterial action in the colon leads to excess formation of ammonia which may be absorbed. Purgatives and laxatives are employed to reduce bacterial growth in the colon.
- C/I: Absolute : Mechanical obstruction of the GI tract, acute surgical conditions such as perforation, haemorrhage, volvulus, paralytic ileus, etc..
Relative : In anxious subjects who are likely to develop habituation and misuse the laxatives.
- P/C: Irritant laxatives should be avoided during pregnancy as these may cause pelvic congestion, although abortion following therapeutic doses of laxatives is most unlikely. Similarly, these drugs should also be avoided in case of typhoid fever and in very ill cardiac patients.
- S/E: Laxatives used occasionally are not harmful but their repeated administration may produce gastro intestinal disturbances like spastic colitis, dyspepsia, anorexia and nausea; nutritional deficiency of calories, vitamins and minerals due to interference with their absorption; loss of fluids and electrolytes particularly potassium and calcium giving rise to hypokalemia and osteomalacia; complete dependence on drugs and later even resistance to all the mild laxatives, due to the development of spastic colon.
- D/I: Laxatives and purgatives may lead to malabsorption of nutrients and drugs if used continuously

Bisacodyl ★

Structurally related to phenolphthaline. Stimulant laxative, acts mainly on the large bowel.

I: Constipation, prior to radiological procedures and surgery.

C/I: Intestinal obstruction, children.

P/C: Should not be given within 1 hour following antacid or milk.

S/E: Increased intestinal motility, abdominal cramps, colonic atony, faecal impaction.

P/A: Tablet 5mg,

Suppositories 5mg, 10mg.

Dose: 5 - 10 mg h.s. (adults), 5 mg h.s. in children or 10 mg rectal suppository in the morning.

D/I: None reported.

Cost: Tab 5mg (10) Rs.9.00

Supp 10mg (5) Rs.25.00-33.00

Senna

Anthraquinone group of laxative. Stimulant laxative acts by stimulation of the large bowel, inhibits sodium chloride and water absorption in colon.

I, C/I, P/C, S/E: Same as the above

P/A: As calcium salts of senna glycosides.

Tablet 12 - 18 mg.

Dose: 2 - 4 tablets at h.s. Maximum 6 tablets daily.

Children over 6 years : 1 - 2 tablets depending on age at h.s.
Maximum 3 tablets daily.

D/I: None reported.

Cost: Tab senna glycosides(as calcium salts) 18 mg (10 x 10) Rs. 64.00

Methyl Cellulose

Bulk laxative. Not absorbed when given orally and increase the indigestible residue. They absorb water, swell up causing stimulation for mechanical distension for evacuation.

I: Relieve constipation by increasing faecal mass

C/I: Intestinal obstruction, colonic atony, faecal impaction.

P/C: Adequate fluid intake should be maintained to avoid intestinal obstruction.

S/E: Flatulence, abdominal distension.

P/A: Only combinations are available. (Syrup)

Dose: 1 g o.d. or q.d.s.

D/I: Not reported.

Cost: Syrup (combinations) 200 mL Rs. 30.00 - 32.00

3. Drugs used in Gastrointestinal Disorders

Agar

It is a mucilaginous substance extracted from marine algae which contains hemicellulose. In contact with water, it forms a gel which has emollient properties and act as bulk laxative.

I, C/I, P/C :, D/I:, Same as above

P/A: Combinations are available

Dose: 4 g h.s.

Lactulose

Osmotic laxative, they hold considerable amount of water thus increasing intestinal bulk which acts as a mechanical stimulus causing increased intestinal motility.

I: Constipation, hepatic encephalopathy. Its metabolite is lactic acid which can bind ammonia and inhibit its absorption.

C/I: Galactosemia, intestinal obstruction

P/C: Young children.

S/E: Flatulence, cramps, and abdominal discomfort.

P/A: Liquid, syrup.

Dose: Constipation : 10 g b.d.

Hepatic encephalopathy : 20 - 30 g t.d.s.

D/I: Not reported.

Cost : Liquid	667mg/mL	(200mL)	Rs.102.00
Syrup	3.325g/5mL	(200mL)	Rs.107.00

Liquid paraffin

Emollient laxative which exerts a softening and lubricating effect on faeces.

I: Constipation.

C/I: Children less than 3 years of age.

P/C: Avoid prolonged use

S/E: Anal seepage of paraffin and consequent anal irritation after prolonged use. Granulomatous reactions caused by absorption of small quantities of liquid paraffin.

P/A: Oral emulsion, also combinations are available.

Dose: 10 - 30 mL h.s.

D/I: Not reported.

Glycerine ✧

Osmotic laxative : Softens and lubricates dried up faeces.

I: Constipation

P/A: Rectal suppository, rectal liquid.

Dose : 3 g for adults, 1 - 1.5 g for children.

Cost : Rectal liquid (enema) 20 mL Rs. 25.00

Magnesium Salts

Osmotic laxatives. Also stimulates intestinal secretory and motor activity. Acts on small and large intestine.

I: Bowel evacuation prior to surgery, radiological procedure, to flush the GI tract in poisoning.

C/I: Acute GI conditions.

P/C: Hepatic and renal impairment, elderly and debilitated.

- P/A & Dose :
1. Magnesium citrate solution - Dose: 240 mL when needed.
 2. Magnesium sulphate - rapid bowel evacuation in 2-3h.
Dose: 5 -10 g with water (granules)
 3. Magnesium hydroxide - liquid - Dose : 10 - 20 mL.

Castor Oil

I: Irritant laxative. Metabolite of ricinoleic acid acts as an irritant and produces purgation. Acts on small intestine particularly used for the preparation of the bowel before contrast urography such as intravenous pyelography.

C/I: Intestinal obstruction.

P/C: Menstruation, pregnancy,

S/E: Nausea, vomiting.

P/A: Liquid

Dose: 5-20 mL when required (best given in milk or fruit juice)

Ispaghula husk

I: Relieve constipation by increasing faecal mass.

C/I: Intestinal obstruction, colonic atony, faecal impaction.

P/C: Adequate fluid intake should be maintained to avoid intestinal obstruction.

S/E: Flatulence, abdominal distension.

P/A: Powder 100 g.

Dose : Adults and children over 12 years : 1 measureful (5.4 g) in morning and at h.s. or 2 measurefuls at h.s.

Children between (6 - 12 years) : Half to one measureful in the morning and at h.s. or 1-2 measureful at h.s.

Children below 6 years : Not recommended except under medical advise.

Cost : Powder 100 g Rs. 30.00 - 37.00

3. Drugs used in Gastrointestinal Disorders

Diocetyl Sodium Sulfosuccinate (docusate sodium)

Emollient laxative.

- I: Reduces surface tension, softens faeces.
- C/I: Intestinal obstruction.
- P/C: Avoided in children, prolonged use can precipitate the onset of an atonic non functioning colon., avoid taking with liquid paraffin as it may increase the absorption of oil.
- S/E: Abdominal cramps.
- P/A: Tablet 100 mg,
Solution 0.25%.
- Dose: 100 - 200 mg t.d.s.
Solution: squeeze contents of the bottle in to the rectum
- D/I: Interfere with potassium-retaining effects of potassium sparing diuretics.
- | | | | | |
|-------|----------|-------|--------|----------|
| Cost: | Tab | 100mg | (10) | Rs. 8.00 |
| | Solution | 0.25% | (50mL) | Rs.19.00 |

3.7 ANTIFLATULANTS

These are drugs prescribed with the hope of relieving the subjective feeling of abdominal distension and fullness after food. Their exact role in vague dyspepsias is not clear. Still they are effective in giving symptom relief.

Simethicone

- I: Antiflatulant, diagnostic aid in gastroscopy and radiography of the bowel.
- C/I: Hypersensitivity.
- P/A: Available in combination with antacids.
- Dose: 40 - 125 mg q.d.s. after meals and h.s., or as needed
- Cost: Not freely available as pure preparations, but available in combination with antacids.

Activated charcoal

- I: Antiflatulant, antidiarrhoeal, antidote for adsorbing ingested poisons.
- C/I: Dehydration, acute dysentery, parasite associated diarrhoea.
- P/C: Do not take any other medication within 2 h of charcoal ingestion.
- S/E: Pain, swelling of abdomen, diarrhoea, vomiting, black stools.
- P/A: Tablet
Powder
- Dose: Antiflatulant 1 - 4 g t.d.s. after meal.
- D/I: Effectiveness of concurrently used medication decreased because of adsorption and increased elimination by the activated charcoal

Simethicone and activated charcoal may be administered as such or as compound tablets along with antacids such as magnesium trisilicate, dried aluminium hydroxide gel, or prokinetic drugs such as metoclopramide, domperidone or cisapride, or digestive enzymes such as fungal diastase, papain. Ingredients which used to be included in carminative mixtures of the past such as cinnamon oil, caraway oil, tincture cardomom oil and sodium bicarbonate also act as antiflatulants. These are seldom used at present.

3.8 PROKINETIC DRUGS

These increase gastrointestinal motility thereby stimulating gastric emptying and small intestinal transit. Hence they are used in reflex oesophagitis and cytotoxic-induced nausea and vomiting.

Metoclopramide

Cisapride

Domperidone

Digestive enzymes

Formulations (tablets, syrup) containing digestive enzyme like pancreatic lipase, papain, fungal diastase, pepsin are available.

I: Absolute indication - Malabsorption syndrome occurring in chronic pancreatic insufficiency, other causes of malabsorption where pancreatic digestion is defective.

Relative indication - vague dyspepsias, flatulence, post diarrhoeal small intestinal dysfunction.

Dose: 1-2 tablet or 5-10 mL after each meal.

3.9 ANTIHAEMORRHOIDAL DRUGS

Haemorrhoids are to be treated surgically for complete relief, but the complications occurring from time to time have to be managed medically. Constipation, local pain and discomfort, inflammation of the pile masses, thrombosis and bleeding constitute the major clinical problems demanding treatment. Regular loss of blood leads to iron deficiency anaemia and in any severe case the anaemia is correctable only after stopping the source of blood loss.

A mild laxative such as liquid paraffin or a bulk laxative such as ispaghula helps to soften the faeces. Inflammation is to be treated with antibacterial agents such as ciprofloxacin or amoxycillin. Pain relief is obtained by an NSAID such as diclofenac or ibuprofen.

Local irritation and inflammation subside with ointments containing lignocaine, zinc oxide, hydrocortisone acetate, peru balsam and pramoxine hydrochloride. The ointment has to be applied into the anal canal and its surroundings, using the applicator provided along with the tube, twice a day once following defecation and once at bed time.

Fissure in ano

This causes intensive pain and local discomfort which demand the use of local anaesthetic application, described under haemorrhoids. Systemic analgesics such as NSAIDs and paracetamol may be required at times. For the relief of spasm of the anal sphincter, antispasmodics such as propantheline bromide has to be employed.

Propantheline bromide

- I: Peptic ulcer, gastritis, spastic colon, ulcerative colitis
- C/I: Glaucoma, GI obstruction, unstable cardiac rhythm, hypersensitivity.
- P/C: Use with caution in pregnancy, lactation, hiatus hernia with reflux oesophagitis, prostatic hypertrophy and pyloric stenosis.
- S/E: Cardiac arrhythmias, toxic megacolon, glaucoma, urinary retension, tachycardia, orthostatic hypotension.
- P/A: Capsules 15 mg
- Dose: Peptic ulcer 30 - 45 mg h.s.
Ulcerative colitis 15 mg t.d.s. before meals.
- D/I: Additive anticholinergic effect with tricyclic antidepressants, phenothiazines and disopyramide.
- Cost: Cap 15 mg (10) Rs. 22.00 - 25.00

3.10 DRUGS USED IN INFLAMMATORY BOWEL DISEASES

(Crohn's disease and ulcerative colitis)

Corticosteroids

Besides oral and parenteral preparations, enemas (including foam preparations) and suppositories containing corticosteroids are available. Hydrocortisone and prednisolone foam enemas are available along with applicators to assist administration of metered dose into the rectum 1-2 times daily for 2-3 weeks.

Sulphasalazine

Mestamine or mesalazine

- I: Ulcerative colitis, Crohn's disease
- C/I: Hypersensitivity
- P/C: Use with caution in pregnancy and lactation. Dose reduction necessary in kidney impairment
- S/E: Nausea, diarrhoea, abdominal pain, GI upsets. rarely thrombocytopenia, neutropenia, hepatitis and nephritis
- P/A: Tablets 250 mg, 400 mg, 500 mg
Enema 60 mL

Dose : Adult 1-2.5 g/day in divided doses.

D/I. Lactulose or other pH lowering drugs may reduce the release of mesalazine at its site of action.

Cost : Tab 250 mg (10) Rs. 100.00 - 110.00

Enema 60 mL (1) Rs. 60.00 - 70.00

Immunosuppresants

Azathioprine

Methotrexate

Anti infective agents - broad spectrum antibiotics

Ciprofloxacin

3.11 DRUGS USED IN THE MANAGEMENT OF ASCITES

Specific treatment depends upon the cause. Symptomatic management is aimed at relieving discomfort due to abdominal distension. In chronic ascites accompanying cirrhosis liver and chronic pancreatitis, general angioedema measures form the mainstay of treatment.

1. Salt restriction - to below 2 g/salt/day.
2. Regular use of diuretics - frusemide in combination with aldosterone antagonist (spironolactone)
3. Limited paracentesis to relieve discomfort.

3.11.1 General approach to administration of drugs in acute and chronic hepatic failure

Most, if not all of the drugs used in modern therapy undergo metabolic transformation in the liver. Therefore the liver is vulnerable to metabolic injury and damage by them. Normal liver has sufficient reserve to carry out this function. When the liver function is impaired due to any reason, drug metabolism becomes deranged. This may lead to accumulation of drugs and their toxic metabolites in the system giving rise to unpredictable effects, eg. prolonged sedative effect of barbiturates in hepatitis.

In addition several drugs cause damage to liver cells, thereby accelerating the hepatic dysfunction and precipitating the occurrence of hepatic failure. Drugs form an important cause for acute and chronic hepatic failure. This occurs in previously normal liver, and in acute or chronic liver disease.

Special caution is needed in prescribing drugs in patients with the following conditions.

Viral hepatitis, drug induced hepatitis, cirrhosis liver, all causes of jaundice, acute and chronic alcoholism and others.

3.11.2 Drugs used in the management of gall stones

Chenodeoxycholic acid

- I: Gallstone disease.
- C/I: Pregnancy, lactation, hypersensitivity, atherosclerosis, biliary cirrhosis, pancreatitis, cholecystitis, hepatic impairment.
- P/C: Determination of hepatic function and ultrasonogram is advised prior to treatment. Serum cholesterol concentration determination recommended at 6 month interval during therapy.
- S/E: Diarrhoea, indigestion, loss of appetite, nausea, vomiting, stomach cramps.
- P/A: Capsule 250 mg
- Dose: 250 mg/day taken with food or milk in the morning and at night.
- D/I: Antacids, colestipol, cholestyramine decrease the absorption of the drug. Clofibrate, oestrogens, neomycin or progestins increase cholesterol saturation of bile thereby decrease the effect of chenodeoxycholic acid.
- Cost: Tab 250 mg (10) Rs. 85.00 - 90.00

Ursodeoxycholic acid

- I: Gallstone disease, biliary cirrhosis, chronic hepatitis and cystic fibrosis.
- C/I, P/C, S/E, D/I: Same as for chenodeoxycholic acid.
- P/A: Tablet 150 mg
- Dose: 8 - 10 mg/kg/day in divided doses, taken with meals.
- Cost: Tab 150 mg (10) Rs. 75.00 - 80.00

3.11.8 Drugs used in diseases of the pancreas

Acute pancreatitis

- Antispasmodics
- Analgesics
- Antibiotics - broad spectrum.

CHAPTER 4 : NUTRITION

4.1 GENERAL CONSIDERATION

4.1.1 Normal nutrient requirements

Nutrient requirements vary depending upon the age, lean body mass, physical activity and special circumstances such as infancy, childhood, adolescence, pregnancy, convalescence from illness and surgical operations. Children, adolescents, pregnant women, and those convalescing from debilitating illnesses and surgical operations require considerably excess of nutrients for tissue building and repair. Energy is expressed as joules (previously referred to as calories).

$$1 \text{ calorie} = 4.184 \text{ joules}$$

For calculating average energy requirements, the concept of reference man and reference woman is adopted. An Indian Reference Man (IRM) is defined as one who is 25 years old, healthy, weighs 55 kg and has surface area of 1.62 m². An Indian Reference Woman (IRW) is defined as one who is 25 years old, healthy, weighs 45 kg and has a surface area of 1.40 m². The basic energy requirement for IRM is 38 kcal/m²/h and for IRW is 32.9 kcal/m²/h.

The National Institute of Nutrition (NIN) Hyderabad has recommended the following energy requirements per day.

	Male 55 kg	Female 45 kg
Sedentary life	2400 kcal	1900 kcal
Moderate activity	2800 kcal	2200 kcal
Heavy physical activity	3600 kcal	3000 kcal

Balanced diets for different age groups are given in tables below.

Table 1
Balanced diet for pre-school children (2 - 6 years)

Food item (g/day)	2 - 3 years		4 - 6 years	
	Vegetarian	Non vegetarian	Vegetarian	Non vegetarian
Cereals	150	150	200	200
Pulses	50	40	60	50
Green leafy vegetables	50	50	75	75
Other vegetables including roots & tubers	30	30	50	50
Fruits	50	50	50	50
Milk	300	200	250	200
Fats & Oils	20	20	25	25
Meat, Fish, Eggs	—	30	—	30
Sugar or jaggery	30	30	40	40

Table II

Balanced diet for school children (7 - 12 years)

Food item (g/day)	7 - 9 years		10 - 12 years	
	Vegetarian	Non	Vegetarian	Non
		vegetarian		vegetarian
Cereals	250	250	320	320
Pulses	70	60	70	60
Green leafy vegetables	75	75	100	100
Other vegetables including roots & tubers	50	50	75	75
Fruits	50	50	50	50
Milk	250	200	250	200
Fats & Oils	30	30	35	35
Meat, Fish, Eggs	--	30	--	30
Sugar or jaggery	50	50	50	50

Table III

Balanced diet for adolescent boys and girls

Food item (g/day)	Boys 13 - 15 years		Boys 16 - 18		Girls 13 - 18 years	
	Veg.	Non	Veg	Non	Veg.	Non
		veg.		veg.		veg.
Cereals	430	430	450	450	350	350
Pulses	70	50	70	50	70	50
Green leafy vegetables	100	100	100	100	150	150
Other vegetables	75	75	75	75	75	75
Roots & tubers	75	75	100	100	75	75
Fruits	30	30	30	30	30	30
Milk	250	150	250	150	250	150
Fats & Oils	30	40	45	50	35	40
Meat, Fish	--	30	--	30	--	30
Eggs	--	30	--	30	--	30
Sugar or jaggery	30	30	40	40	30	30
Ground nuts		50*	50*			

* An additional 30 g fats and oils can be added in place of ground nuts.

Table IV

Balanced diet for adult men and women**(Figures in brackets give the requirement for women)**

Food item (g/day)	Sedentary work		Moderate work		Heavy work	
	Veg.	Non veg.	Veg.	Non veg.	Veg.	Non veg.
Cereals	400 (350)	400 (350)	475 (350)	475 (350)	650 (475)	650 (475)
Pulses	70 (60)	55 (45)	80 (70)	65 (55)	80 (70)	65 (55)
Green leafy vegetables	100 (125)	100 (125)	125 (125)	125 (125)	125 (125)	125 (125)
Other vegetables	75 (75)	75 (75)	75 (75)	75 (75)	100 (100)	100 (100)
Roots & tubers	75 (50)	75 (50)	100 (75)	100 (75)	100 (100)	100 (100)
Fruits	30 (30)	30 (30)	30 (30)	30 (30)	30 (30)	30 (30)
Milk	200 (200)	100 (100)	200 (200)	200 (100)	200 (200)	100 (100)
Fats & Oils	35 (35)	40 (35)	40 (35)	40 (40)	50 (40)	50 (45)
Meat, Fish	-- --	30 (30)	-- --	30 (30)	-- --	30 (30)
Eggs	-- --	30 (30)	-- --	30 (30)	-- --	30 (30)
Sugar or jaggery	30 (30)	30 (30)	40 (30)	40 (30)	55 (40)	55 (40)
Ground nuts	-- --	-- (40)	-- --	-- --	50* (40)	50* --

* An additional 30 g fats and oils can be added in place of ground nuts.

Note : During pregnancy and lactation an allowance of 50 - 100 cereals, 10 g pulses, 25 g leafy vegetables, 125 mL milk, 15 g fats and 10 - 20 g sugar is to be added.

Daily allowance of nutrients for Indians
(Nutrition expert group of ICMR 1968)

Group Particulars	Energy (cal.)	Proteins (g)	Calcium (mg)	Iron (mg)	Retinol (mcg)	Thiamine (mg)	Riboflavine (mg)	Nicotinic- acid (mg)	Ascorbic acid(mg)	Folic acid (mcg)	Vit B12 (mcg)-	VitD IU
Man												
Sedentary work	2400	55	400-500@	20	750	1.2	1.3	16	50	100	1	200
Woman												
Sedentary work	1900	45	400-500@	30	750	1.0	1.0	13	50	100	1	200
Children												
1 year	1200	17	400-500*	15-20	250	0.6	0.7	8	30-50	55-100	0.5-1	200
2 years	1200	18	400-500*	15-20	250	0.6	0.7	8	30-50	55-100	0.5-1	200
3 years	1200	20	400-500*	15-20	250	0.6	0.7	8	30-50	55-100	0.5-1	200
4-6 years	1500	22	400-500*	15-20	300	0.8	0.8	10	30-50	55-100	0.5-1	200
7-9 years	1800	33	400-500*	15-20	400	0.9	1.0	10	30-50	55-100	0.5-1	200
10-12 years	2100	41	400-500*	15-20	600	1	1.2	14	30-50	55-100	0.5-1	200
Adolescent boys												
13-15 years	2500	55	600-700+	25	750	1.3	1.4	17	30-50	55-100	0.5-1	200
Adolescent girls												
13-15 years	2200	50	600-700+	35	750	1.1	1.2	14	30-50	55-100	0.5-1	200

Note: * New US recommendation 1200 mg
+ New US recommendation 1200 mg
@ New US recommendation 800 mg

Table VI
Weight and height chart for males and females

Height (cm)		Normal Weight (kg)		Over weight limit (+20%)		Underweight limit(-20%)	
M	F	M	F	M	F	M	F
148	148	47.5	46.5	57.0	56.0	38.0	37.0
152	152	49.5	48.5	59.0	58.0	39.0	39.0
156	156	51.5	50.5	62.0	60.5	41.0	40.5
160	160	53.5	52.5	64.0	63.0	43.0	42.0
164	164	56.0	55.0	67.0	66.0	45.0	44.0
168	168	59.0	58.0	71.0	69.6	47.0	46.5
172	172	62.0	60.5	74.5	72.5	49.5	48.5
176	176	65.5	64.0	78.5	77.0	52.4	51.0
180	180	68.5	67.0	82.0	80.5	55.0	53.5
184	184	72.0	70.5	86.5	84.5	57.5	56.5
188	188	75.5	74.0	90.5	89.0	60.5	59.0
190		77.5		93.0		62.0	

Note : M: Males

F: Females

Locally available natural articles of food should be preferred since they are more cost effective and acceptable. All cases of malnutrition, irrespective of whether they present as generalised or predominantly specific nutritional deficiency, should be considered as having generalised nutritional inadequacy with more pronounced deficiency of the specific nutrient. This statement is true except in a few instances of conditioned deficiencies such as INH induced pyridoxine deficiency or antibiotic induced B-complex deficiency. It is therefore necessary to manage all nutritional deficiency disorders with total dietary correction supplemented by therapeutic administration of the specific nutrient. It should be remembered that since most of the nutrients are stored in the body, every nutritional disorders manifest only when the stores are totally depleted.

Treatment with the specific nutrient rapidly corrects the clinical disorder but it requires prolonged administration to build up the stores. It is therefore necessary to continue treatment for further periods after correction of the clinical disorder and give proper dietary advice in order to prevent relapse.

4.1.2 Specific instances where supplemental nutrition should be instituted

Infancy

Prolonged breast feeding without introduction of other items of food beyond 5 - 6 months may lead to iron deficiency.

Adolescent girls

They may lose varying amounts of blood due to frequent and heavy menstrual periods and thereby develop iron deficiency, unless medicinal iron is given.

Pregnancy

The Nutritional requirements are considerably increased during pregnancy. There is great demand for additional calorie, proteins, calcium, iron and other nutrients required for the foetus, placenta and maternal tissues to grow. The foetus draws its requirement from the mother's nutritional stores. So the mother's nutritional status is likely to go down, especially if repeated pregnancies occur at short intervals without adequate nutritional supplementation. Additional provision for pregnancy should include calories, proteins, vitamins, minerals like iron and calcium and fresh fruits and vegetables which also provide bulk.

Acute illness

Prolonged fever, surgical operations, post traumatic states and such other conditions are associated with excess of catabolism which leads to rapid weight loss and development of nutritional deficiencies. The problem is often complicated by loss of appetite which impairs food intake. During those periods provision of high caloric, easily digestible and palatable foods such as milk and milk products, sugar, fruit juices, honey, commercially available protein supplements and others help to compensate for the hypercatabolic states, at least partially. When oral intake of food and fluids is not possible either due to coma or local conditions in the upper gastrointestinal tract, feeding has to be done through Ryle's tube. The optimum amounts of fluid, calories, proteins, minerals and vitamins have to be given through the Ryle's tube.

For an adult, a day's supply should include :

Milk 600 mL or commercial milk substitutes 100 g

White of 3 eggs.

Sugar 200 g.

Rice or wheat 100 g; made into kanji, boiled and homogenised in a mixer and strained with a cloth so that the same may be given through a Ryle's tube.

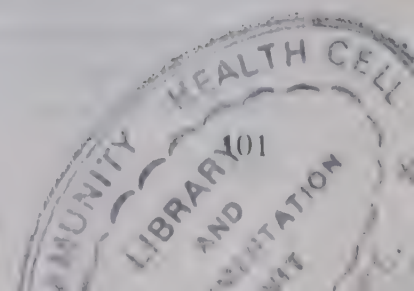
Common salt 6 - 8 g

Multivitamin tablet - 1

Fruit juice - equivalent of 3 oranges or 2 limes

Potassium chloride - 2 g.

D12-400
07026



Water to make upto a total of 2.5 L of fluid.

Locally available popular articles such as tender coconut water, sugarcane juice, butter, milk etc are very pleasant and acceptable sources of calories and nutrients but since their composition varies from time to time they should not be relied upon in critical situations.

Elderly subjects

Persons above the age of 70 years are likely to suffer from nutritional deficiencies due to various causes such as loss of the teeth and anorexia which impair food intake. Chronic illnesses, economic dependency and neglect from relatives worsen the problem. In such cases proper advice is given to family members on appropriate diets and provision of dietary services by social and voluntary organisations go a long way to solve this problem. They particularly require 1000 iu of Vit D daily to prevent excessive osteoporosis and osteomalacia.

4.1.3 Staple diets

Carbohydrates

Rice, wheat, maize and oats and tubers such as tapioca (cassava), yam, potatoes and others provide calories and bulk for the food. Any one of them may be used depending on the availability and taste. On an average cereals consist of 80 % of carbohydrates, 7 - 10% proteins and small amounts of fats. Whole meal cereals contain B-complex factors and are also rich in fibre content. Tubers such as tapioca and yam are poor in proteins.

C/I : Allergic conditions : The particular item of food should be avoided. In coeliac disease and gluten induced enteropathy, wheat and rye should be avoided. During post diarrhoeal states there may be temporary suppression of intestinal enzymes such as lactase and sucrase. During these periods lactose, sucrose and such other carbohydrates aggravate the diarrhoea. Therefore they have to be avoided.

P/C : In diabetes unrestricted supply of cereals and sugars should be avoided.

Proteins

Requirement of proteins is modified considerably by the dietary habits, especially the staple diet. For a predominantly cereal based diet such as ours the protein requirement is 1 g/kg/day. Articles which are rich in proteins include milk and dairy products, fish, meat, other animal foods etc. Peanuts, cashewnuts, jackfruit seeds and soya beans are excellent sources of vegetable proteins. Cereals such as rice and wheat contain proteins. In dietaries which include large quantities of cereals (300 - 400 g/day) they provide adequate amounts of proteins.

Table VII

Protein content of common articles of diet.

<u>Name of article</u>		<u>% w/w</u>
Rice		6.8
Wheat		11.8
Egg	Hen	11.8 - 12.2
	Duck	13.9
Fish		15.0 - 24.0
Meat		10.9 - 51.4
Ground nut		26.7
Soyabean		43.2

I: Dietary proteins are vital and they are essential components of food for the maintenance of growth, tissue repair, anabolic activities and immunological processes. If proteins are given without adequate carbohydrates to maintain energy requirements, the former will be used up as energy sources and they will not fulfill the anabolic needs.

C/I: Allergic states against particular proteins. Among dietary articles proteins are the most common sources of mild or serious forms of allergy.

P/C :1. Proteins should be given in optimal amounts. Excess proteins should be avoided since they do not provide any extra benefit other than providing sources of energy. Moreover proteins are more expensive than carbohydrates. In the presence of renal insufficiency and hepatic insufficiency excess or even normal amounts of proteins lead to metabolic complications. So protein intake has to be tailored to the functional reserve of these organs and the metabolic needs.

2. There are several inherited disorders involving enzymes participating in the metabolism of nitrogen in the body eg. phenylketonuria, cystinuria, cystinosis, orotic aciduria etc.

Special dietary measures have to be adopted in such cases

Supplemental proteins

When dietary proteins cannot be ingested normally as during acute illnesses, surgical operations and the like, protein concentrates which are commercially available and which contain about 20% of native or pre-digested protein can provide the daily requirement.

Protein concentrates derived from milk proteins, soyabean proteins or animal proteins are commercially available for oral use. The dose has to be individualized.

Amino acid solutions

Essential aminoacids are available as parenteral solutions. When given intravenously they form good supplementary sources of nitrogen and they also stimulate protein anabolism. They contain a mixture of essential and non-essential synthetic aminoacids.

Average composition of the available aminoacid solutions is given below :

Composition of intravenous aminoacid solutions

Nitrogen g/L	Electrolytes mmoles / L				
	Potassium	Magnesium	Sodium	acetate	chloride- others.
8 - 24	25-30	2.5	35	53-109	31-67

Administration : i.v. infusion over 1 - 2 hrs daily for 3 - 5 days or more

Caution : Anaphylactic reactions.

P/A : i.v. injection 20 mL and i.v. infusions 200 mL, 500 mL.

Cost : Inj (20 mL) Rs. 25.00
 Inf (200 mL) Rs. 160.00 - 205.00
 Inf (500 mL) Rs. 240.00

Fats

These add taste to the food and so they have found increasing use in the dietary with the improvement in economic status and with different culinary practices. All articles of food except probably green vegetables contain fats in appreciable amounts. Rich sources include milk and milk products, fish liver, animal livers, red meat, animal fats, oils, oil seeds and nuts. Except fish oils, animal fats are generally saturated fats and excess or even moderate consumption of these tend to raise serum cholesterol in susceptible individuals. Vegetable oils except coconut oil and red palm oil generally contain unsaturated fatty acids and these are devoid of the risk of inducing hypercholesterolemia and consequent atherosclerosis.

Fats are the main sources to provide additional calories in hyperalimentation regimens instituted during periods of hypercatabolism.

I: Absolute : When high caloric diets are needed.

Relative : To add taste and quality of food.

C/I : Fat malabsorption states, chronic pancreatitis, allergic states, obesity.

P/C : Diabetes, hypertension, abnormalities of lipid metabolism, ischaemic heart diseases.

Atheromatous, occlusive arterial disease may be adversely affected if care is not taken to control the quantity and quality of the fat.

In general the preparations available for artificial nutrition are highly expensive and their cost amounts for a considerable proportion of the expense incurred for bone marrow transplantation over chemotherapy.

4.2 VITAMINS

4.2.1 Fat soluble vitamins

Vitamin A

Also known as retinol - which is chemically a primary alcohol. One international unit (iu) is equivalent 0.344 mcg of pure all - trans vitamin A acetate and this corresponds to 0.6/mcg of all trans beta carotene.

Sources:

Milk and milk products, liver, green leafy vegetables, fish liver oils, lemon grass oil etc. In human beings vitamin A is stored in the liver. Sunlight causes deterioration of the vitamin and therefore Vitamin A has to be kept in amber colored bottles. Precursor of vitamin A is carotene which is present in green vegetables, tomatoes, papaya, pumpkin, carrots, mangoes, red palm oil and several others. It is converted into Vit A in the small intestinal mucosa and other tissues. Vit A is stored in the liver.

Normal daily requirement in health is 2000 - 3000 units, (700 - 1000 mcg) varying with age - 750 mcg for adults, 1000 mcg during pregnancy and lactation and 300mcg for infants.

Therapeutic doses go up to 20000-50000 units per day depending upon the clinical state.

- I: Vit A is an essential component of normal diet and should be provided as natural food.

Therapeutic indications for Vit A preparations

1. Deficiency states.
2. Prophylactic against xerophthalmia and keratomalacia

In susceptible communities Vit A should be given prophylactically for the prevention of xerophthalmia, in single doses of 1,00,000 units orally under direct supervision at 6 months intervals.

Other probable indications

1. As prophylactic against recurrent respiratory infection and urinary tract infections. Oral doses 4000 to 10,000 units given on a long term basis, are beneficial.
2. In chronic liver disease conversion of carotene into Vitamin A and storage are defective and so overt Vitamin A deficiency may develop. Either daily oral doses of 3000 units of Vit A or injection of 1,00,000 units once in 3 months may be given.
3. Retinoic acid is used as a topical application as a cream or gel in the treatment of acne vulgaris.

P/C: High doses given continuously lead to hypervitaminosis A. Excessive ingestion of carotene leads to carotinemia and discolouration of tissues, this condition is self-limiting on withdrawing carotene.

An overt eye signs of Vit A deficiency demand urgent administration of large doses of Vit A in order to prevent blindness.

In emergency indications such as keratomalacia 50,000 - 1,00,000 units of Vit A palmitate should be given as deep i.m once in a week for 4 -6 weeks followed up with daily oral dosage or in injections of 1,00,000 units every month. For infants and children the dose is 50,000 units i.m. monthly.

Continued prolonged use of Vit A in doses above 10,000 units daily may give rise to hypervitaminosis A.

P/A : Oral : Tablets, capsules, fish liver oil capsules and drops containing vitamin A and D.

Preparations for paediatric use -Drops, malt preparations, which also contain Vit D, iron and calcium, and syrup preparations containing several nutrients.

Parenteral preparations: Vitamin A palmitate available for deep i.m. injection

Cost: Cap 50,000 iu (30) Rs. 36.00 - 37.00

Vitamin D (calciferol) - anti-rachitic vitamin ✧

This is the precursor of the metabolically active product 1, 25 hydroxy Vit. D

Natural Sources

Vit D is synthesised in vivo in the skin by the action of ultraviolet light (from sun light) on its precursor cholesterol.

Dietary sources : It is obtained from several animal foods such as milk, milk products, liver oils, fish, liver, egg, yolk and others. Liver and liver oils are particularly rich sources. The Vitamin exists in the form of ergocalciferol

In health the two sources supplement each other. In tropical climates, moderate exposure to sun is adequate to provide the requirement, but in places where exposure to sunlight is minimal, dietary sources are more important. The Vitamin, obtained from either source has to undergo metabolic conversion into 25 - hydroxy Vitamin D in the liver and thereafter into 1, 25 dihydroxy Vit D which is the metabolically active product. In liver diseases and in chronic renal disease these conversions may be defective and therefore secondary deficiencies of Vit D may manifest. In such conditions dietary provision of Vit D may not be adequate 1,25 hydroxy Vit. D may have to be given orally or parenterally. Daily requirement of Vit. D is 400 iu/day (ie) 10 mcg.

P/A : Oral : Most of the available preparations contain a mixture of Vit D, Vit A, calcium lactate and other nutrients as well. In this form Vit D is available as tablets, drops, fish liver oils, capsules, syrup form and malt preparations.

Parenteral - Oil-based preparations are available for i.m. injection. Effect of one dose lasts for 3 months.

Cost :	Tab	0.25 mcg	(10)	Rs. 104.00
	Cap	0.25 mcg	(15)	Rs. 256.00
	Inj	300000 iu	(3 x 1 mL)	Rs. 17.50 - 25.00

- I: Vit D is an important component in nutrition and therefore several infant foods, cereals and other natural foods are fortified with small amounts of Vit D. In the absence of Vit D, rickets develop in children, and in adults the disease takes the form of osteomalacia and also osteoporosis.

Elderly subjects require 400-600 iu of Vit D daily to prevent osteomalacia and osteoporosis.

Urgent indications: Rickets in children and osteomalacia in adults. This responds to oral doses of Vit D 1000 - 2000 iu / daily. Alternatively a single i.m. injection of 6,00,000 units may be given for advanced cases. The effect of one injection lasts for upto 3 months. 3-4 injections are given at intervals of 3-4 weeks. If the condition does not clear up after 2-3 injections, the condition should be considered as Vit. D resistant rickets.

Malabsorption states: Injection of Vit D are required.

Treatment of hypercalcemia: Vit D is given orally in dose of 1500 to 5000 units for 2-4 weeks and thereafter the dose is reduced. Pharmacological doses of 40,000 units (1 mg) are required to correct hypocalcemia caused by malabsorption states and upto 1,00,000 units may be needed to correct the hypocalcemia of hypoparathyroidism. In these two conditions Vitamin D should be given i.m.

1, 25 - hydroxy Vitamin D

- I: Chronic liver disease and chronic renal failure benefit only if this preparation is administered. It is available as alpha calcidol and calcitriol in the form of capsules containing 250 nanograms or injections containing 2 mcg/mL.

C/I: Any cause of hypercalcemia, metastatic calcifications, urinary stone disease worsened Vit. D.

P/C: Regular ingestion of large doses of Vit.D in excess of 10,000 units/day lead to hypervitaminosis-D. There is no risk of hypervitaminosis from increased exposure to sun light. In caucasians excess sunlight may predispose to the development of cutaneous melanoma.

P/A:	Cap	0.24 mcg	(10)	Rs. 70.00
		1.0 mcg	(10)	Rs. 245.00
	Tab	0.25 mcg	(10)	Rs. 104.00

Dose: Oral : 1 - 2 capsules /day

Injection :- i.v. or i.m. 500 nanogram thrice a week.

Pharmacological doses of Vit D tend to produce hypercalcemia. Therefore regular monitoring of serum calcium levels at monthly intervals is required. The dose has to be withdrawn or reduced if the serum calcium exceeds 11 mg/dL. 1,25 hydroxy Vitamin D has a shorter half life compared to Vit D and therefore the serum calcium levels come down promptly on withdrawing the drug.

Cost: Tab 0.25 mcg (10) Rs. 104.00 - 105.00

Cap 0.25 mcg (10) Rs. 70.00 - 75.00

Vitamin E (alpha tocopherol)

Natural sources : wheat germ oil vegetable oils, egg yolk, butter, peas, cotton seeds.

Daily requirements : 15 iu (5 mg)

Vit. E functions as an antioxidant and probably acts to preserve the integrity of cell membranes.

- I: There are no clearcut definite indications since nutritional deficiency is rare. In premature infants fed on artificial diets containing iron and high concentration of fatty acids conditioned deficiency of Vit E may occur leading to the development of haemolytic anaemia.

At present Vit E is prescribed widely as an antioxidant in several chronic degenerative diseases such as atherosclerosis, neuromuscular disorders and other ailments in the elderly.

C/I: Allergy, gastric intolerance and unpleasant taste due to eructations of the drug.

P/C: Vit E is safe even when given for prolonged periods.

P/A: Capsules 200 mg, 400 mg

Drops 50 mg/mL

Pearls 400 mg.

Dose: Variable 1 - 2 capsules may be given after food.

Cost: Cap 400 mg (10) Rs. 22.00 - 23.00

Drops 50 mg/mL (15 mL) Rs. 16.00 - 18.00

Pearls 400 mg (10) Rs. 18.00 - 21.00

Vitamin K - coagulation vitamin ☆

Daily requirement 70 - 140 mcg / day.

It is a naphthaquinone. Several molecular forms exist

Vit K1 - (phytomenadione) - (phylloquinone) this is present in vegetable oils and

green leafy vegetables.

Vit K2 - Synthesised by colonic bacteria in varying amounts, this supplements the dietary sources.

Vit K1 & K2 are fat soluble. They can be given orally or by i.m. injection.

Vit K3 - is a synthetic Vit K, available in water soluble form. It can be given orally, i.m. and i.v.

In the liver Vit. K is mainly concerned with the synthesis of the active forms of prothrombin, factor VII, IX and X, protein C and protein S, all concerned with haemostasis.

Vit. K is required for the formation of several proteins concerned

with calcium homeostasis and bone metabolism.

Since normal diets contain adequate amounts of Vit K and also the colonic microbes synthesise it, there is no need to supplement Vit K normally. Vit. K deficiency leads to bleeding tendency.

- I: Oral anticoagulants overdosage with bleeding tendencies, prolonged obstructive jaundice, malabsorption states, premature new borns, prolonged starvation, conditioned deficiency in antibiotic therapy.

P/C : Large doses especially in the new borns may give rise to haemolytic anaemia.

P/A: Oral tablets : Water soluble preparation menadiol sodium phosphate - 10 mg.

Phytomenodione 10 mg tablets.

Parenteral phytomenadione for slow i.v. injection 2 mg/mL and 10 mg/mL.

Dose : In an emergency caused by bleeding due to overdose of anticoagulants Vit K₁ (natural) has to be given i.m. in doses of 10 mg, to be repeated later depending upon the response. If the bleeding tendency is severe 50 - 75 mg may be required. Other measures such as transfusion of plasma fraction or even fresh whole blood may be required.

In haemorrhagic states and in malabsorption states Vit K₁ may be given i.m.

The synthetic preparation can be given i.v. in doses of 5 to 10 mg daily.

Cost : Tab 0.66 mg (10) Rs. 15.00

4.2.2 Water soluble vitamins

Vitamins B₁ (thiamine, aneurin) ☆

This acts as conenzyme in the metabolism of carbohydrates. Its requirement is dependant on the amount of carbohydrate ingested.

Source : Cereals (maximum concentration is just adjacent to the bran), sprouting pulses, green leafy vegetables, liver, pork and legumes. Cooking does not destroy the vitamin, but discarding the boiled water, and excessive washing causes loss. Daily requirement 0.4 mg/1000 k.cal ingested or about 1.2 mg/day.

Deficiency produces cardiac and circulatory disturbances (cardiac beriberi) and neurological manifestations which may present as chronic sensorimotor polyneuritis or the acute neurological emergency - Wernicke's encephalopathy.

- I: It is an essential and vital component of human nutrition.

Therapeutic indications - Thiamine deficiency manifestations as wet beriberi or dry beriberi

Dose is 50 mg given i.m. or i.v. followed by oral. Dosage of 10-50 mg daily for several months.

In Wernicke's encephalopathy thiamine has to be given as an emergency measure in doses of 50-100 mg, i.v. over a period of 10 minutes.

P/C : Thiamine given by injection may give rise to sensitization and anaphylactic shock.

P/A : Tablets : 25 mg, 50 mg, 100 mg.

Injection : 100-250 mg

Multivitamin infusions containing ascorbic acid, nicotinamide, pyridoxine hydrochloride, riboflavine and thiamine hydrochloride.

Multivitamin tablets - Thiamine hydrochloride 15 mg, riboflavin 15 mg, nicotinamide 50 mg, pyridoxine hydrochloride 10 mg and Vit C 100 mg.

Dose : Oral 10 - 100 mg daily as a single dose after food.

Parenteral - 100-250 mg for deep i.m. or i.v.

Cost :	Tab	75 mg	(4 x 10)	Rs. 42.00
	Caps	5 mg	(250)	Rs. 35.00
	Inj	100 mg/mL	(10 mL)	Rs. 17.00

Vitamin B2 (riboflavin) ☆

It takes part in oxidation - reduction reactions concerned with tissue oxidation and respiration. Daily requirement 0.60 mg/hour cal (ie) 1.5-2 mg/daily.

Natural Sources: Liver, Meat, eggs, kidney, milk, other dairy products, leafy vegetables, sprouted cereals and pulses. The Vitamin is moderately heat resistant, but boiling in alkaline media destroys the vitamin, so also sunlight. Deficiency causes vascularization of the cornea. Oculo-rogenital syndrome may occur.

I : It is an essential component of normal nutrition.

Therapeutic indications: Signs of deficiency - dose 2-10 mg daily - available as riboflavine tablets or in combination with the other members of B- complex group and Vit C.

Parenteral preparation for i.m. or i.v. use - 10 mg either singly or along with other vitamin.

P/C : Allergic reactions.

P/A : Tablet 20mg

Dose	Prophylactic	1 to 4 mg daily
	Therapeutic	5 to 10 mg daily

Cost :	Tab 20 mg	(10)	Rs. 5.00
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Vitamin B₃ (niacin, nicotinic acid, nicotinamide) - Antipellagra vitamin

It acts as a coenzyme in the metabolic pathway of carbohydrates and proteins.

Natural Sources : Liver, pulses, whole cereals, fish, meat, groundnuts, milk, egg, coffee and to a smaller extent vegetables. Partial loss of the vitamin occurs during cooking. Deficiency of the vitamin leads to pellagra. Though the fullfledged form manifests with dermatitis, diarrhoea and dementia a wide spectrum with mild to severe manifestations occur. Strong clinical suspicion is needed to diagnose mild cases.

I: Niacin is an essential component of normal nutrition.

Therapeutic indications : Signs of deficiency states, dose 100 mg oral b.d., or t.d.s. for 2-3 weeks.

Dyslipidemias : In a dose of 100 mg t.d.s., nicotinic acid is a cheap, but very effective drug to produce mild to moderate reduction in serum cholesterol and triglycerides compared to gemfibrozil and the cost is much less.

F/C : Nicotinic acid tablets and injections may give rise to a feeling of flushing over the eyes and mouth, paraesthesia and pruritus. This is harmless and usually wanes off on continued use.

Patients should be reassured, otherwise it may lead to non-compliance.

P/A : Tablet 50 mg, 100 mg.

Injection 50 mg, 100 mg.

It is a common ingredient of multivitamin tablets and injections.

Dose : Prophylactic Oral : 15-30 mg daily.

Therapeutic Oral : i.v. 50 - 250 mg daily.

Vitamin B₆ (Pyridoxine) ☆

Active form of this vitamin is pyridoxal. It acts as a coenzyme in the metabolism of aminoacids and biological amines such as catecholamines and 5-hydroxytryptamine. It is also required for the biosynthesis of gamma amino butyric acid in the brain.

Sources: Yeast, liver, meat, whole-grain cereals, peanuts, legumes and bananas.

Daily requirement: 1.25 mg.

Under ordinary circumstances nutritional deficiency of this vitamin is uncommon. Conditioned deficiency occurs in treatment with INH, oral contraceptives and hydralazine. Clinical features include dermatitis, cheilosis, angular stomatitis, glossitis, dizziness, vomiting and peripheral neuropathy. Infantile convulsions and a form of sideroblastic anaemia have been attributed to pyridoxine deficiency.

I: 1. Deficiency states : dose 10 mg/day oral.

2. Prophylactic administration of pyridoxine 6 mg when INH is given in doses of 300 mg/day or more.

3. In sideroblastic anaemia high doses of 100 mg b.d. or t.d.s. may be required.

P/C: High doses of pyridoxine may impair the efficacy of INH.

P/A: Tablets 10 mg, 50mg, 100 mg.

Dose : Oral : 10, 50 or 100 mg or as per the indication.

Parenteral dose: i.v. 50 mg often in combination with other B-complex factors.

D/I: It reduces the efficacy of L-dopa given for parkinsonism if administrated concurrently.

Cost : Tab 40 mg (10) Rs. 4.00 - 5.00

Tab 100 mg (10) Rs. 14.00 - 15.00

Pantothenic acid

A member of the B-complex group, this vitamin is widely distributed in animal and vegetable foods and therefore dietary deficiency is extremely rare. It acts as a coenzyme in the body. Daily requirement is 4 - 7 mg/day. In experimental animals deficiency leads to dermal and hair changes, neuromuscular degeneration and fatal adrenal haemorrhage.

- I: As a nutritional supplement in extreme malnutrition, and during parenteral nutrition.

Empirically calcium pantothenate has been used to stimulate intestinal motility in paralytic ileus and to reduce neurotoxicity of streptomycin.

P/A: Only with other Vitamin B constituents in syrup form.

Dose : Oral : Calcium pantothenate 50 - 100 mg/day i.v.

Biotin

It is an organic acid functioning as coenzyme in several carboxylation reactions. It is present widely in several articles of food. Intestinal microbial flora also synthesis biotin.

Daily requirement is about 100 - 200 mcg.

Naturally occurring deficiency state is rare. Conditioned deficiency may occur in food fads who consume excessive amounts of egg white. So also infants fed on parenteral nutrient solutions develop biotin deficiency characterised by lassitude, irritability, sensory disturbances, anorexia, rashes and hair loss.

Inherited disorders of biotin metabolism may be rarely encountered in neonates and infants. They respond dramatically to large oral supplements of biotin in a dose of 5 - 10 mg daily.

Vitamin B₁₂ (cyanocobalamin) ✧

It is a cobalt containing water soluble vitamin. Along with folate, it takes part in DNA synthesis. Pathological effects of Vit. B₁₂ deficiency include abnormalities of DNA synthesis in several tissues in the body. The prominent

clinical manifestations are megaloblastic erythropoiesis, neurological abnormalities including disturbances of higher functions and abnormalities of the function of the corticospinal tracts and posterior columns presenting as subacute combined degeneration of the spinal cord.

Sources: This Vitamin is obtained mainly from animal sources, liver and meat being rich in B₁₂. Vegetable articles of diet and milk are poor sources. Adequate amounts are obtained from fermented milk and similar dairy products, buttermilk, curd, yoghurt and cheese. Contamination of water supplies by coliform bacteria provide minimal amounts of the vitamin in many areas.

Daily requirement : 1 mcg. Up to 1 mg or more of the Vitamin can be stored in the liver and made available during periods of short supply and therefore clinical manifestations of deficiency develop only on dietary deprivation lasting for several months to years. In India the more common causes of deficiency are dietary inadequacy, chronic destructive lesions of gastric mucosa and malabsorption states. In the Caucasian races commoner cause is pernicious anaemia in which there is atrophy of gastric mucosa and absence of intrinsic factor in the stomach. Other rare causes include abnormalities of transcobalamins and interference with Vit B₁₂ metabolism by drugs like phenytoin sodium.

I : Vit B₁₂ is an essential component of human nutrition. Vegans and food-fads who do not take foods of animal origin including dairy products require oral supplementation. In many parts of India combined deficiency of iron, folate, Vit B₁₂ and several other factors is responsible for nutritional megaloblastic and dimorphic anemias. Combination therapy with iron, folate and Vit B₁₂ is needed in such cases to get ideal results.

Therapeutic indications : Clinical features of Vit B₁₂ deficiency.

Megaloblastic anaemia, neurological abnormalities, post gastrectomy states, malabsorption states, pernicious anemia.

Parenteral : Possible indications : prophylaxis against post-herpetic neuralgias 1 mg i.m. 2-3 injections during the acute phase of herpes zoster and early convalescence.

i.m. or i.v. 1 mg week x 3-4 weeks Supplemented by oral dose of 10 mcg day in whom absorption is normal.

In these in whom absorption and metabolism are defective, the dosage has to be continued at monthly intervals parenterally.

P/C : Apart from local and generalized allergic reactions, which are mild, no serious toxic effects are known.

P/A : Tablets 1 mcg, 2 mcg, 10 mcg.

Often with other members of B-complex vitamins especially thiamine and pyridoxine.

Multivitamin syrup

Injection available for i.m. or i.v. use cyanocobalamine and hydroxocobalamin 1 mg/mL.

Dose : Megaloblastic anaemia i.m. - 1 to 2 mg in divided dose for 1 week, followed by a maintenance dose of 250 mcg weekly till blood count is normal.

D/I: Alcohol amino salicylates or colchicine reduce absorption of Vit. B12. Folic acid large and continuous doses may reduce Vit B12 concentration in blood.

Cost : Tab 250 mg (10) Rs. 9.00
Inj 100 mcg/mL (5 mL) Rs. 12.00

Folic acid ☆

Chemically it is pteroyl glutamic acid and in natural foods it exists as polyglutamates. It takes part in the metabolism of nucleic acid - Deoxy ribonucleic acid. Deficiency leads to abnormalities in several tissues, most prominently manifested as megaloblastic anaemia, glossitis and dark pigmentation of the skin. Dietary deficiency is common in India. 30-40 % of nutritional anaemias have folate deficiency as well. Deficiency state develops within weeks of dietary deprivation.

Sources : Liver, meat, yeast, green leafy vegetables, sprouted cereals and legumes, nuts, chocolates.

Folic acid is lost by boiling in large volumes of water for prolonged periods.

Daily requirement 50-100 mcg.

Requirement is higher in children and pregnant women.

I: Folic acid is a vital component of human nutrition.

Therapeutic indications : Deficiency states megaloblastic anaemia.

Dose oral tablets 5-20 mg/day over prolonged periods.

Prophylactic Indications: During pregnancy - 1 mg daily oral. (200 - 500 mcg/day)

As a protective against neural tube defects - 5 mg daily oral during the early months of pregnancy.

In heavy anticonvulsant therapy, in order to prevent development of megaloblastic anaemia

300 mcg/day oral to 5 mg/day to 5 mg/daily.

P/C : Higher doses impair efficacy of anticonvulsant medication

P/A : Tablets 5 mg folic acid

Tablets and syrup along with other components of the B complex group and Vit C.

Cost : Tab 5 mg (10) Rs. 6.00 - 8.00

Vitamin C (ascorbic acid) - antiscorbutic vitamin ☆

It is a strong reducing agent participating in oxidation reduction reactions. It takes part in the synthesis of collagen and metabolism of the erythrocyte. Body stores are limited

Source : Fresh fruits, leafy vegetables, citrous fruits, germinating pulses
During cooking the vitamin may be lost partially.

Deficiency symptoms occur early when the diet is deficient

Daily requirement : for infants 5 mg/kg bw
 for adults 30-40 mg/day.

Deficiency states : Children - 300 mg/day
 Adult - 1g/day.

Deficiency of Vit C leads to several nonspecific manifestations such as susceptibility to infections, fatigue, malaise etc. Advanced deficiency leads to classic scurvy characterized by several foci of bleeding and follicular keratosis

P/C : Anaphylactic reactions.

S/E : Oral dose may produce digestive disturbances

In doses exceeding 3 g/day hypoglycemia may occur

Prolonged use of large dose may lead to the development of oxaluria and oxalate urinary stone formation.

P/A : Tablet : 500 mg.

Drops, Injection 100 mg.

Dose : Oral : 25 - 500 mg given orally daily depending on the condition

Cost : Tab 500 mg (10) Rs. 8.00 - 9.00

Drops 100 mg/mL (15 mL) Rs. 8.00 - 9.00

Inj 100 mg/mL (5 mL) Rs. 6.00 - 7.00

4.3 MINERAL SUPPLEMENTATION

In normal persons taking a balanced diet selective deficiency of trace elements and minerals does not occur and therefore supplementation is not necessary.

Administration of mineral salts can be considered under two heads :

1. As a part of nutritional supplementation either prophylactically or curatively. eg. Calcium in osteomalacia and osteoporosis, iron salts in iron deficiency anaemia, iodine in endemic goitre.
2. As replacement therapy in mineral depleted states, often along with other components such as water which are also simultaneously depleted. This form of replacement therapy is aimed at providing required amount of mineral and fluid at the appropriate rate with a view of restoring the milieu interior to normal.

eg. Sodium chloride and water in dehydration,

Potassium chloride in hypokalemia,

Calcium gluconate in hypocalcemia,

Sodium bicarbonate in acidosis.

4.3.1 Nutritional requirement of minerals

Sodium Chloride (common salt)

The requirement for an adult is 8 - 12 g per day. This depends partly on the climatic conditions and physical exertion. In hot and humid environment where sweating is profuse larger amounts are required. Salt is an essential component of most of the natural foods. Natural salt obtained from the sea contains several other minerals such as iodine, and trace elements.

In several countries including India iodised salt is provided which contains 15 ppm of sodium iodide, as a prophylactic measure against iodine - deficiency disorders.

In communities where the general level of salt intake is higher, prevalence of systemic arterial hypertension is also higher.

P/C: In conditions such as cardiac failure and chronic renal disease salt intake has to be closely monitored.

P/A: i.v. injection : sodium chloride 0.9% (normal saline) or different strengths. Normal saline 500 mL available in polythene bags with the i.v. infusement.

Glucose saline (1:1 mixture of isotonic sodium chloride and 5 % glucose)

Ringer lactate (sodium- 131, potassium -5, calcium -2, bicarbonate (as lactate) 29, chloride-111) mmol/L.

Potassium

This is normally obtained from diet, drinking water, vegetables, fruits and meat products and others. Daily requirement is 4 - 12 g 50 - 150 mmol and this is adequately supplied by dietary sources.

Potassium supplementation is necessary in hypokalemic states and while providing total enteral or parenteral nutrition. Nutritional purposes, provision of 2-4 g potassium chloride daily is adequate.

P/C: Hyperkalemia leads to cardiac arrest and hypokalemia leads to muscle paralysis. Both are serious potentially fatal complications. So administration of potassium has to be monitored carefully, especially when given parenterally.

In patients with oliguric renal failure, hyperkalemia may develop even from dietary potassium or oral supplements.

P/A: Potassium chloride : oral tablets 500 mg

Potassium chloride slow release tablets : 600 mg

Potassium chloride: 7.5% in syrup.

Effervescent potassium tablets containing the benzoate, bicarbonate and/or chloride equivalent of 500 mg potassium chloride

i.v. potassium chloride containing 1.5 g in 10 ml (20 mmol to be given i.v. added to 500 mL Sodium chloride or 5% glucose solution)

Potassium 2 - 4 g ~ 25 to 50 mmol.

Calcium

Normally obtained from milk, dairy products, meat and vegetables. One litre of milk contains 12 g calcium, and an egg contains 30 mg. Daily requirement is 500 mg for adults, 1000 mg for pregnant, lactating and postmenopausal women and 700 mg for children and adolescents.

1. Oral tablets or syrups - as nutritional supplement in vulnerable groups.

Treatment of osteomalacia and osteoporosis 1000-1500 mg daily oral for several months.

Emergency measures:

1. Acute hypocalcemic tetany
1 or 2 ampoules of calcium gluconate are given i.v. as push doses over 3-5 min. This is followed up by giving calcium gluconate 1 g oral b.d. or as i.v. drip for prolonged periods.
2. Urticaria.
3. Severe intractable pruritus.
4. To mitigate the ill effects of hyperkalemia.

C/I: Any cause of hypercalcemia and metastatic calcification, chronic renal failure, digitalis administration.

P/C: i.v. calcium produces a sense of heat and flushing during the injection. This is generally harmless and self limiting. The patient has to be reassured. Calcium salts if they extravasate from injection sites lead to severe pain, extensive necrosis and chronic ulceration.

P/A: Calcium gluconate : 600 mg equivalent of 53.4 mg of elemental calcium.

Calcium lactate : 300 mg tablet equivalent of 39 mg calcium.

Calcium carbonate : effervescent tablets or chewable tablets or granules all containing

1.25 - 2.5 g (equivalent of 500 - 100 mg calcium)

Calcium salts in combination with Vit D as tablets or syrup.

Parenteral preparations : Calcium gluconate 10% solution equivalent to 8.9 mg calcium (229 micromol) per mL.

Calcium chloride 10% solution 100 mg/mL equivalent to 27.3 mg calcium (ie) 680 micromol/mL

Magnesium

Nutritional deficiency is extremely uncommon except in those on prolonged total starvation or those with malabsorption states.

Therapeutic Indications

1. In parenteral and total enteral nutrition.
2. Hypomagnesemia.
3. Cardiac arrhythmias especially in ventricular tachycardia.
4. Eclampsia - 4 g i.v. given over 20 min.
5. As a purgative 10 - 15 g/oral on an empty stomach.

P/C : Chronic liver disease

Proper monitoring of all vital parameters should be available when magnesium is given parenterally.

P/A : Oral Magnesium sulphate - tablets or as mixture 1-2 g/day
magnesium glycerophosphate tablet

Injection : Magnesium sulphate 50% (2 mmol/mL).

Dose : Oral Magnesium sulphate - tablets or as mixture 1-2 g/day.

Parenteral: Magnesium sulphate 50% (2 mmol/mL) either to be given as i.v. infusion in a dose of 24 mmol in 24 hrs or as a slow i.v. injection of 8 mmol on 10-15 min.

Iron

It is an essential component of normal nutrition, taking part in the formation of haemoglobin, myoglobin and also several vital enzymes in all tissues. Major proportion of body iron is stored in the liver, marrow and other tissues. In the absence of bleeding sources, considerable period should elapse between the onset of dietary deficiency and development of deficiency symptoms. Iron deficiency manifests as vague ill health and subtle disturbances of function of several systems. Classic manifestations include hypochromic microcytic anaemia, koilonychia and sideropenic dysphagia (Plummer Vinsen syndrome)

Sources : Rich sources are animal foods like meat, liver, kidney, fish and egg yolk. Fruits, onions, green vegetables, cereals, pulses, oilseeds, jaggery, raisins, grapes, apricots and dates contain iron. Betel leaf is an especially rich source. Milk is a poor source. Ground water and iron cooking vessels provide good amounts of iron in many communities. Animal proteins and ascorbic acid enhance the absorption of iron. Haemoglobin and myoglobin iron present in animal food is better absorbed (11-22%) than the iron from vegetable sources (1-7%). The bioavailability of iron from the average dietary of Indians is low and therefore twice or even thrice the recommended allowance has to be provided to prevent iron deficiency in susceptible groups such as pregnant women and those with chronic blood loss.

- I: Iron is essential component of normal nutrition. When a balanced diet is taken, in the absence of any abnormal - blood loss, medicinal iron is not necessary.

Iron deficiency anaemia : Oral iron salts are indicated.

Daily requirement : 10 - 20 mg for men and 30 - 40 mg for women.

Infants require 1 mg/kg bw

Prophylactic administration to prevent iron deficiency states

1. Pregnancy, lactation, repeated pregnancies.
2. Premature infants and infants fed predominantly on milk formulas beyond 6 months of age.
3. Elderly subjects whose diet is likely to be inadequate

Therapeutic iron administration : The aim of oral therapy is to provide 200

mg of elemental iron daily. Various preparations are available. They are similar in efficacy, but varying in cost and side effects. Ferrous sulphate is the cheapest and most widely available preparation. It may cause more of unpleasant side effects in a few who may not be able to tolerate the drug, but the vast majority tolerate it well.

Indications for parenteral iron :

1. When the haemoglobin has to be brought up to normal levels with in a shorter period.
eg. pre operatively or when anaemia is detected in the later months of pregnancy.
2. Malabsorption states.

P/A:	Preparation of iron salts	Tablet	Elemental iron	Dose
	Ferrous sulphate	200 mg	65 mg	tab t.d.s. soon after meals
	Ferrous sulphate (hydrated)	300 mg	60 mg	"
	Ferrous fumarate	200 mg	65 mg	"
	Ferrous gluconate	300 mg	35 mg	"
	Ferrous succinate	100 mg	35 mg	"

Chelated iron

Ferrous glycine sulphate - 5 mL containing 25 mg elemental iron.

Polysaccharide iron complex 5 mL containing 100 mg iron.

Sodium iron edetate 190 mg containing 27.5 mg iron.

Compound preparations - tablets or syrups in combination with other minerals and vitamins.

S/E: Nausea, vomiting, epigastric pain, diarrhoea or constipation and an astringent taste in the mouth. Side effects are less if iron is given after food, but absorption is also less when compared to administration on empty stomach.

P/A: (liquid form) For paediatric use drops, syrups, or malts are available containing iron salts in combination with other nutrients.

Several preparations such as slow-release granules have been formulated. Their advantages are only slight, if any. Gastric delivery system is a new technology in which the iron is enclosed in a capsule which becomes semipermeable, releasing small quantities of iron, at the same time remaining in the stomach for a much longer periods.

Injection : Iron dextran complex contains elemental iron 50 mg/mL.

Iron sorbitol complex contains 50 mg iron/mL.

Dose & routes of administration: Deep i.m. injection in a dose of 100 mg elemental iron.

For total dextran complex (IMFERON) equivalent to 500 to 1000 mg elemental iron is added to 500 mL 5% glucose and given as a slow intravenous drip over 2-3 hrs. Since the chances of anaphylactic reactions are high, proper pre-infusion testing with 0.1 mL of the drug i.m., and one hour later again i.v. should be done. For the first 15 minutes the drip should be given very slowly (20 - 25 drops) per minutes and therefore at a moderate rate (30 - 40) drops per min. Medical attendance and resuscitatory measures should be available throughout the infusion and for 6 hrs there after.

Calculation of dosage for i.m. and i.v. administration.

Total dose of iron required in mg = weight of the patient in kg \times Hb in % \times 0.66

Once this dose of iron is administered, no further iron is needed. The body takes its own time to incorporate the iron into haemoglobin and restore the haemoglobin levels.

Anaphylactic shock which may be fatal, rigor, sinking feeling, local pain over the site of injection, thrombophlebitis, convulsions, pyrexia, arthralgia, arthritis, serum sickness like reactions, and local pigmentation over injection sites. If oral iron is administered concurrently those reactions are more frequent. Therefore, oral iron preparations should be stored at least a week before giving parenteral iron.

Iodine

This is an essential component of normal nutrition required for the formation of thyroid hormone.

Sources : Sea salt, sea fishes, vegetables, drinking water and milk.

Daily requirement is 150 - 250 mcg

Iodine deficiency is prevalent over wide geographical zones in India including several pockets in Kerala and a wide spectrum of iodine deficiency disorders are seen in these areas.

Prophylaxis : Iodisation of salt with 10 PPM of sodium iodide is done as a public health measure as a national policy.

Therapeutic indications:

1. Prophylaxis of iodine deficiency disorders - use of iodised salt regularly, or i.m. injection of iodized oil containing 500 mg of iodine once in three years.
2. Thyrotoxicosis - Lugol's iodine or potassium iodide pre operatively - dose 60-100 mg/day.
3. Thyroid crisis. Sodium iodide i.v. injection dose of 300 - 600 mg, 8h

P/C : Pregnancy, lactation.

S/E : Hypersensitivity reactions including upper respiratory allergy.

conjunctivitis, pain over the salivary glands, rashes and iodism

P/A : Lugol's iodine : 5 % iodine dissolved in 10% potassium iodide dose 0.1 to 0.3 mL t.d.s. diluted with water or milk.

Iodine content 10 mg in each drop. Potassium iodide saturated solution contains 50 mg iodine in each drop.

Sodium iodide solution for intravenous use contains not more than 0.1 % of sodium thiosulfate or other suitable reducing agent and contain a buffer.

4.4 ARTIFICIAL NUTRITIONAL SUPPORT

4.4.1 Oral diets and nutritional supplements

Foods with different flavours and increased caloric contents and acceptability have a role to play in improving nutrition during convalescence from illness. In chronic intestinal failure, though the intestinal functions can recover to some extent by adaptation, the reduction in digestive and absorptive capacity limits their usefulness.

Enteral tube feeding : This method delivers the nutrient directly into the stomach or intestine. It is needed for patients who are unable to eat or swallow. When tube feeding is envisaged for periods only up to four weeks small bore nasogastric tubes (Ryles or others) may be used.

Gastrostomy : Percutaneous gastrostomy tubes are introduced either endoscopically or surgically and these deliver the nutrient directly into the stomach.

With proper care of the gastrostomy this method can be continued for several months.

Solutions for enteral feeding: Peptide solutions with added medium chain triglycerides are absorbed well. These supply energy, and also help to restore intestinal function. Specific additives modify intestinal function and recovery eg. glutamine promotes intestinal recovery and immunological function, omega-3 fats suppress inflammatory response.

Delivery of nutrients through enteral tube should be properly controlled, preferably using an infusion pump. Only about 180 mL/hour will be tolerated by the stomach. Monitoring of glucose levels and electrolyte balance should be instituted for optimal response.

P/A : Amino acids with minerals and multi vitamins.

Essential aminoacid with multivitamins.

Cost : Amino acids with minerals and multi vitamins

(50 g (sac) Rs. 60.00 - 170.00

Essential aminoacid with multivitamins

(10) Rs. 29.00 - 30.00

4.4.2 Parenteral nutrition

This is the method by which nutrient supply is achieved through a venous access, probably using an infusion pump. If the duration is less than two weeks a peripheral vein may be used. If longer, central venous catheter should be used. Different types of catheters are available for this purpose.

1. Inability to ingest and digest the food through the alimentary tract.
2. Pre-operative and post-operative states.
3. Patients with intestinal failure.
4. Severe cases of hyperemesis gravidarum.
5. Intensive cancer chemotherapy.
6. Bone marrow transplantation.
7. Severe burns.

Nutrient solutions

This should contain sufficient calories, nitrogen, vitamins, minerals and adequate fluid. Total non-protein energy supply should be 25-40 cal/kg bw. This is provided in the form of glucose and lipid in the proportion of 150-250 Cal/g of nitrogen supplied. The lipid provides 30 - 50% of total non protein calories and consists mostly of long chain triglycerides. Nitrogen is provided as crystalline amino acid solutions at the rate of 0.25 - 0.3 g/kg bw. All vitamins, electrolytes and trace elements such as selenium and chromium are included in the solution.

Complications include sepsis, blockage of catheter and other mechanical problems.

After an initial period of hospitalization and training of the patient and their attendants parenteral nutrition can be organized in their homes and domiciliary treatment can be continued.

F/A: Injection: essential amino acid + glycine, sorbitol 20 mL Rs. 25.00
 Inf Minerals, essential and non-essential (200 mL) Rs. 160.00 - 202.00 amino acids

Cost: In general the preparations available for artificial nutrition are highly expensive and this cost accounts for a considerable proportion of the expenses incurred by bone marrow transplantations, cancer chemotherapy, etc.

Topical NSAIDs may provide some slight relief of pain in musculoskeletal conditions. These should be applied with gentle massage. Avoid contact with eyes, mucous membrane and inflamed and broken skin. Discontinue if rashes develop. They are not to be used with occlusive dressings. Not generally suitable for children.

CHAPTER 5: DRUGS USED IN CARDIOVASCULAR DISORDERS

5.1 ANTI ARRHYTHMIC DRUGS

Antiarrhythmic drugs are used in the treatment of cardiac arrhythmias. They are classified into various groups by their mechanism of action. The classification is known as the Vaughn Williams classification.

5.1.2 Classification

Class 1 drugs

- Quinidine, disopyramide, procainamide.
- Lignocaine, phenytoin, mexiletine, tocainide
- Flecainide, encainide, propafenone, moracizine (ethmozine).

Class 2 drugs

Betablockers

Class 3 drugs

Amiodarone, sotalol, bretylium, N-acetyl procainamide

Class 4 drugs

Calcium channel blocking drugs.

Unclassified : Adenosine, ATP, digoxin.

Drugs used in treatment of supraventricular tachyarrhythmias :

Adenosine, verapamil, diltiazem, esmolol, metoprolol, amiodarone, digoxin, propafenone.

Drugs used in the treatment of ventricular arrhythmias :

Lignocaine, phenytoin, mexiletine, amiodarone, betablockers, quinidine, disopyramide, procainamide.

5.1.2.1 Class 1a drugs

Quinidine ★

I: Supraventricular arrhythmias, ventricular arrhythmias.

C/I: QT prolongation, AV block.

P/C: Avoid intravenous administration as it may cause hypotension
Cardiac conduction abnormalities, proarrhythmia and AV block are to be looked for.

S/E: Cinchonism, allergic reaction, thrombocytopenia, haemolytic anaemia, proarrhythmia.

P/A: Quinidine Sulfate Tab 300 mg

Quinidine Gluconate Inj 76 mg of quinidine/ml.

Dose : Oral: 200-400 mg t.d.s. If necessary to be increased to 600 mg every 2-4 hrs.

Parenteral: 600 mg initially, then 400 mg repeated every 2-6 h if necessary. 800 mg i.v. infusion. The i.v. dose may cause hypotension and therefore to be diluted and administered with ECG and B.P. monitoring. Due to the severe risk of hypotension this drug is seldom used now.

D/I: Increases serum digoxin level.

Note: *Start with 100 mg initially to avoid hypotension.*

Cost: Tab 100 mg (20) Rs. 36.00

Disopyramide

I: Ventricular and supraventricular arrhythmias.

C/I: AV block, sinus node dysfunction, severe cardiac failure.

P/C: Hepatic and renal impairment, glaucoma, heart failure, elderly patients, pregnancy.

S/E: Hypotension, myocardial depression, AV block, dryness of mouth, urinary retention, blurring of vision.

P/A: Capsules 100 mg, 150 mg.
Tablets 100 mg.

Dose: 100 - 150 mg 8 th hrly.

D/I: Increased risk of ventricular tachycardia (Torsade de pointes) if used along with class 3 agents, diuretics and erythromycin. May worsen heart failure if used with other negative inotropic agents.

Cost: Cap 100 mg (10) Rs. 51.00 - 52.00

Procainamide ☆

I: Ventricular arrhythmias, atrial arrhythmias usually resistant to other drugs.

C/I: Severe renal failure, heart block.

P/C: Elderly patients, pregnancy, renal dysfunction, hepatic dysfunction, myasthenia.

S/E: SLE like syndrome, nausea, diarrhoea, fever, myocardial depression.

P/A: Capsules 250 mg
Injection 100 mg / mL.

Dose: 250 - 500 mg, initial dose 1 g followed by 500 mg 3 hrly for 24 - 48 hrs then reduce dose to 500 mg t.d.s.

Intravenous dose 100 mg i.v. bolus, followed by 10 - 20 mg/min to a maximum of 1 g in the first hour. Maintenance dose is 1 - 4 mg/min. Due to the high incidence of adverse side effects procainamide should be given as i.v. infusion diluted with 5% glucose at a rate not exceeding 25-50 mg/min until the arrhythmia has been suppressed or a maximum dose of 1 g has been reached.

D/I: Potentiates the action of neuromuscular blocking agents, impairs

5 : Drugs used in Cardiovascular Disorders

action of neostigmine and pyridostigmine. Cimetidine increases the renal clearance of procainamide.

Cost:	Cap 250 mg	(10)	Rs. 38.00 - 39.00
	Inj 100 mg/mL	(10 mL)	Rs. 35.00 - 36.00

5.1.2.2 Class 1b drugs

Lignocaine ✧

I: Ventricular tachycardia.

C/I: S-A block, severe myocardial depression.

P/C: Hypotension, renal and hepatic dysfunction, elderly patients

S/E: Paresthesia, drowsiness, confusional states (especially in old people), convulsion

P/A: Injection 2%, 21.3 mg/mL.

Dose: 1 mg/kg as a bolus dose upto a maximum of 100 mg, along with initiation of continuous infusion 2 mg/min which can be increased to 3 mg/min.

D/I: Increased hepatic clearance in patients receiving cimetidine, propranolol and halothane.

Note: Routine administration of lignocaine is not recommended in acute myocardial infarction as a prophylactic for ventricular arrhythmias.

Cost: Inj 2% (30 mL) Rs. 12.00 - 13.00

Mexiletine ✧

I: Ventricular arrhythmias (mainly in ventricular tachycardia.)

C/I: Sick sinus syndrome, high grade AV block, hypotension.

P/C: Hepatic dysfunction, elderly patients.

S/E: Nausea, confusion (elderly patients), bradycardia, paresthesia, convulsions, ataxia, psychiatric disorders.

P/A: Tablets 150 mg

Injection 250 mg vials.

Dose: Oral dose 150 mg 8 hrly Maximum daily dose upto 1200 mg.

Intravenous 100 - 250 mg at a rate of 25 mg/min.

D/I: Phenytoin and rifampicin increase the metabolism. Diuretics decrease the action through the production of hypokalemia.

Cost: Caps 150 mg (10) Rs. 168.00 - 169.00

Inj 250 mg (10 mL) Rs. 37.00 - 38.00

Diphenyl hydantoin (Phenytoin)

I: Ventricular arrhythmias, digitalis toxicity.

C/I: A.V block, acute intermittent porphyria.

P/C: Hepatic impairment, pregnancy.

S/E: Nausea, vomiting, dizziness, headache, tremor, peripheral neuropathy, ataxia, slurred speech, drug induced lupus erythematosus, gum hypertrophy, erythema multiforme, megaloblastic anaemia.

Dose : 100 mg 8 th hrly.

D/I: Antibiotics, analgesics, amiodarone and antidepressants usually increase the plasma concentration of phenytoin. Phenytoin decreases the concentration of disopyramide, quinidine and mexiletine. Oral contraceptive effect is reduced.

5.1.2.3 Class 2 Drugs - Betablockers (See section 5.7.3)

5.1.2.4 Class 3 drugs

Amiodarone ☆

I: Mainly in refractory life threatening arrhythmias like ventricular tachycardia, atrial fibrillation in WPW syndrome and in prophylaxis of ventricular and supra ventricular arrhythmias not responding to usual line of management.

C/I: Pregnancy, breast-feeding, severe bradycardia, conduction abnormalities, hypo / hyperthyroidism

P/C: Check liver function tests, thyroid functions periodically. Chest X-ray should be checked before and periodically, use with caution in elderly patients and in renal dysfunction, and in bradycardia and conduction abnormality.

S/E: Skin and corneal microdeposits, peripheral neuropathy, photosensitivity, pulmonary fibrosis, hepatic enzyme elevation, haemolytic anemia, aplastic anaemia, hypo or hyperthyroidism, bradycardia, conduction abnormalities.

P/A: Tablets 100 mg and 200 mg
Injection i.v. 50 mg / mL ampoules.

Dose: 200 mg 8th hrly for the first week, 200 mg b.d. for the second week, 100-200 mg o.d., subsequently. The dose should be the minimum effective strength in view of the marked side effects and toxicity of amiodarone. Intravenous administration 5 mg/kg over 20 min - 2h by slow i.v. infusion. May cause hypotension if given rapidly. Alternate dose 150 mg given as bolus i.v. followed by 900 mg slow i.v. infusion for 24 hrs.

D/I: Enhanced anticoagulant activity due to decreased metabolism of anticoagulants, increased action of other antiarrhythmic drugs, increased risk of severe bradycardia with beta blockers and calcium channel blockers, increased risk of arrhythmias with antidepressants, increased serum digoxin level, hypokalemia induced by diuretics may worsen amiodarone toxicity, increased risk of hypothyroidism with lithium.

5 : Drugs used in Cardiovascular Disorders

Note: Amiodarone has a half life of 30 - 110 days and the action of the drug will persist for upto 50 days after stopping treatment. Amiodarone is not to be started as a first line drug as far as possible.

Cost: Tab 200 mg (10) Rs. 40.00 - 89.00
Inj 50 mg/mL (3 mL) Rs. 46.00 - 49.00

Sotalol

Beta blocker with anti arrhythmic activity (class 3)

I: Ventricular arrhythmias, supraventricular arrhythmias including paroxysmal atrial fibrillation.

C/I: AV block, congestive cardiac failure, sick sinus syndrome.

P/C: Congestive heart failure, vasospastic angina, bradycardia, occlusive arterial disease, diabetes mellitus, pregnancy, breast feeding, Raynauds disease.

S/E: Cold peripheries, bradycardia, insomnia, bronchospasm, conduction abnormalities.

P/A: Tablets 40 mg, 80 mg

Dose: 80 - 160 mg b.d.

Lower doses can be tried in certain cases.

D/I: Can worsen bradycardia if combined with digoxin, verapamil, diltiazem, (can induce AV block in some cases). Masks hypoglycemia symptoms if used with hypoglycemic drugs in diabetic patients. Worsen heart failure in patients in combination with other negative inotropic agents.

Cost: Tab 40 mg (10) Rs. 12.00 - 13.00

Other class 3 drugs like bretylium and N-acetyl procainamide are not freely available in India.

Bretylium

Dose: i.m. or slow i.v. injection 5 - 10 mg/kg as a 5% solution repeated in 1-2 h if arrhythmia persist and subsequently every 6-8 h for upto about 3 - 5 days.

5.1.2.5 Class 4 Drugs - Calcium channel blockers

5.1.2.6 Positive inotropic agents

Positive inotropic agents are drugs that increase the contractility of the myocardium. They are useful in the treatment of patients with hypotension and congestive cardiac failure. The positive inotropic agents can be divided into:

- a) cardiac glycosides - digoxin
- b) phosphodiesterase inhibitors
- c) parenteral inotropic sympathomimetics.

Cardiac glycosides

Main action of cardiac glycosides are to increase myocardial contraction and to prolong the conduction in the AV node. The proto type of cardiac glycosides in clinical use is digoxin, though there are various other preparations available.

The current indication of digoxin is in congestive cardiac failure and supra ventricular arrhythmias. Various methods of administration of digoxin has been described;

- a. Rapid parenteral digitalisation
- b. Rapid oral digitalisation
- c. Maintenance dose.

In most cases of mild heart failure a maintenance dose of digoxin is all that is required. Children require a higher dose of digoxin based on body weight, when compared to adults.

Digoxin has a large number of side effects and has a narrow therapeutic to toxic level ratio. Hence the physician administering digoxin should be constantly on the look out for digoxin toxicity. Electrolyte imbalance especially hypokalemia should be avoided as it can worsen digitalis toxicity.

Digoxin ☆

Positive inotropic drug, anti arrhythmic drug.

- I: 1) Congestive cardiac failure especially with atrial fibrillation.
Usefulness in sinus rhythm and congestive heart failure is not as impressive as with atrial fibrillation.

- 2) Supra ventricular tachyarrhythmia particularly atrial fibrillation

C/I: AV Block(intermittent or complete), supraventricular arrhythmias in Wolf. parkinson-White syndrome, hypertrophic cardiomyopathy, sick sinus syndrome.

P/C: Not useful in heart failure due to diastolic dysfunction, constrictive pericarditis, thyrotoxicosis, myocarditis. Use carefully in elderly patients, cor pulmonale, renal impairment, hypokalemia.

S/E: Vomiting, nausea, anorexia. Most common side effects diarrhoea, abdominal pain, visual disturbances (xanthopsia), confusion, fatigue, and hallucinations. Digoxin can produce almost every type of cardiac arrhythmias except Mobitz's type-II AV block. The commonest arrhythmias is ventricular ectopy, but the characteristic arrhythmias of digoxin toxicity are bidirectional ventricular tachycardia and paroxysmal atrial tachycardia with AV block and junctional tachycardias.

D/I: Amiodarone, quinidine, diltiazem, verapamil, nifedipine, and captopril can increase the serum levels of digoxin and cause toxicity. Digoxin dose should be reduced if there is concomitant administration of these drugs. Anion exchange resin can decrease serum digoxin levels. Diuretics can produce hypokalemia and worsen digoxin toxicity. Concomitant administration of betablockers or verapamil can cause marked bradycardia or AV Block.

5 : Drugs used in Cardiovascular Disorders

P/A:	Tablets	0.25 mg,
	Elixir	50 mcg / mL.
	Ampoules	250 mcg/mL 2 mL ampoules.
Dose:	Maintenance oral dose	0.25 mg daily 5 days a week (skip two days a week to avoid cumulative toxicity)
	Rapid oral digitalisation	1 mg in divided doses over 24 h (0.5 mg stat, 0.25 mg 6 h later and 12 hrs later)
	Intravenous digitalisation	250 - 500 mcg over 20 - 30 min (never give rapid i.v. bolus) followed by lower doses 6 h later - total dose not to exceed 1 mg / 24 h.

In general practice, maintenance dose of digoxin is only required in most clinical situations. Parenteral digitalisation is not recommended now due to the availability of better drugs to control the acute situations.

Note : Treatment of digoxin toxicity

- In all patients receiving digoxin a careful watch should be kept for the development of side effects and digoxin should be stopped if there is any suspicion.*
- Precipitating factors like hypokalemia, other drugs etc. should be sought for and treated.*
- The drug of choice for digoxin induced cardiac arrhythmias is phenytoin.*
- In centres where facilities are available, antibodies against digoxin. (Fab antibodies) can be administered to treat digoxin toxicity successfully.*

Cost:	Tab 0.25mg	(10)	Rs. 2.00-6.00
	Elixir 0.05mg/mL	(30mL)	Rs.22.00
	Inj 0.5mg/2mL	(10mL)	Rs.20.00

5.1.2.7 Phosphodiesterase inhibitors

Amrinone, milrinone, vesnarinone

are drugs which have been tried in trials as positive inotropic agents.

These drugs are currently not available in India and hence clinical experience is limited.

5.1.2.8 Sympathomimetic positive inotropic drugs

The beta stimulant drugs used as positive inotropic agents include dopamine, dobutamine and isoprenaline. Earlier drugs used for this purpose included noradrenaline and adrenaline, noradrenaline has peripheral vasoconstriction action due to alpha stimulation, adrenaline has both alpha and beta action. These two drugs are not as frequently used now with the availability of dopamine and dobutamine. Dopamine and dobutamine act on the beta-1 receptors of the myocardium and increase myocardial contractility

The response of dopamine is dose dependent as at higher doses (greater than 5 mcg / kg / min), it acts as a vasoconstrictor and may be deleterious.

Dopamine hydrochloride ☆

Sympathomimetic drug. Positive inotropic agent.

I: Severe hypotension not responding to routine management including correction of hypovolemia.

C/I: Pheochromocytoma, tachyarrhythmias.

P/C: Treatable causes of hypotension should be identified and corrected.

S/E: Hypertension, tachycardia, ventricular ectopics.

P/A: Injection 200 mg vial

Dose: 2-5 mcg/kg/min initially note that at doses above 5 mcg/kg/min renal vasodilating effect is lost.

D/I: MAO inhibitors prolong and increase dopamine effects. Ergot potentiates the vasoconstrictor action of dopamine. Cyclosporine and halogenated hydrocarbon anaesthetics may sensitize myocardium to dopamine and precipitates severe arrhythmias.

Cost: Inj 200mg (5mL) Rs.21.00

Dobutamine ☆

Synthetic sympathomimetic drug.

I: Inotropic support in situations with hypotension. In chronic refractory heart failure intermittent administration of dobutamine has been found to be effective.

Compared to dopamine, dobutamine causes less increase in heart rate, lesser incidence of ventricular ectopy and reduces pulmonary capillary wedge pressure.

C/I: Similar to dopamine

S/E: Hypertension, tachycardia, ventricular ectopy.

P/A: Injection 50mg/4mL, 250mg/5mL, 250mg/20mL

Dose: 2.5 - 10 mcg/kg/min adjusted according to clinical / haemodynamic response.

Available as 250 mg vials.

D/I: It antagonises the effect of phentolamine and prazosin.

Cost: Inj 250mg/5mL (5mL) Rs.335.00

Isoprenaline (Isoproterenol) ☆

Sympathomimetic amine

I: Hypotension associated with complete heart block, severe bradycardia.

C/I: Hypertension, angina pectoris, acute left ventricular failure, halothane anaesthesia.

P/C: Hyperthyroidism, coronary artery disease, diabetes mellitus

S/E: Hypotension, sweating, tremor, headache.

5 : Drugs used in Cardiovascular Disorders

P/A : Tablet 20mg,

Injection 2 mg/mL 2 mL ampoules,

Inhalation 400mcg 200 metered dose

Dose : 0.5 - 10 mcg/min. Available as 2 mL ampoules containing 1 mg/mL.

D/I : With digitalis glycosides and levodopa risk of cardiac arrhythmia. Reduction of antianginal effects of nitrates.

Cost : Tablet 20mg (10) Rs.9.00

Injection 2mg/mL (2 mL) Rs.6.00

Inhalation 400mcg (200 metered dose) Rs.88.00

Other sympathomimetic amines that are used include norepinephrine and epinephrine (adrenaline)

5.2 DRUGS USED IN TREATMENT OF ANGINA

5.2.1 Nitrates

Nitrates are mainly venodilators. They have also dilating effects on epicardial coronary arteries. They are useful drugs in angina pectoris, especially in the treatment of acute anginal episodes. Intravenous nitroglycerin can be used in acute myocardial infarction and unstable angina and also in the control of acute elevation of blood pressure and in left ventricular failure.

Glyceryl Trinitrate ✧

It acts as antianginal and antihypertensive drug. It reduces the preload and afterload and thereby acts as an effective drug in the management of left ventricular failure.

I: Treatment of acute anginal episode, acute LVF, to reduce BP in markedly elevated blood pressure such as hypertensive crisis.

C/I: Hypersensitivity to nitrates, hypovolemia, hypertrophic obstructive cardiomyopathy, aortic stenosis, cardiac tamponade, head injury, closed angle glaucoma.

P/C: Renal disease, hepatic disease, hypothyroidism. Glyceryl trinitrate loses potency when stored for more than 6 months and should preferably be kept away from sunlight. Nitrates especially i.v. nitrate injection should be used with caution in acute inferior wall MI with right ventricular infarction with hypotension.

S/E: Most common side effect is headache. Flushing, postural hypotension causing giddiness, and tachycardia may occur. Development of tolerance : Many patients on regular nitrate therapy become tolerant to the drug after several weeks. Continuous i.v. infusion results in tolerance leading to decreased effectiveness within 24 h. Development of tolerance can be prevented by giving nitrates in eccentric dosing so as to produce long (10 - 12 h) nitrate free intervals or by administration of drugs like captopril which contain -SH group.

P/A: Tablets, buccal spray, transdermal preparation and i.v. infusion.

Tablets: 0.5 mg, 2.6 mg and 6.4 mg long acting.

Transdermal preparation: 2.5 mg, 5 mg, 10 mg and 15 mg released over 24 h.

Ointment: 2% skin ointment contains 15 mg per inch.

Buccal spray: metered dose of 400 mcg.

i.v. infusion as 5 mg and 25 mg vials, 1 mg/mL or 5 mg/mL.

Dose: Oral: • 0.5 mg sublingually for angina.

2.6 mg - 6.4 mg b.d. for long action

Parenteral: i.v. administration: One vial is to be diluted in 500 mL normal saline prior to i.v. infusion and infused at a rate of 10 - 200 mcg/min depending upon the response. Low dose nitroglycerine therapy is preferable and effective compared to high dose infusions in many clinical situations. Careful monitoring of blood pressure essential. To prevent nitrate tolerance, give nitrate at eccentric dosage intervals. eg. 8 am - 1 pm. Transdermal preparation should not be used continuously for more than 12 h.

D/I: Tricyclic antidepressants and disopyramide may reduce action of nitrates. The effect of heparin is reduced by increasing excretion of heparin.

Cost:	Tab	0.5 mg	(30)	Rs. 12.00 - 17.00
	Cap	2.5 mg	(50)	Rs. 80.00 - 90.00
	Inj	25 mg/5mL	(5 mL)	Rs. 45.00 - 50.00
	Oint	30 mg	(2 %)	Rs. 35.00 - 36.00
	Patch	5 mg	(24 hrs)	Rs. 43.00 - 55.00

Isosorbide Dinitrate

It is an antianginal drug is also useful for treatment of heart failure.

I: Chronic angina pectoris, prevention of acute episodes of angina.

C/I, P/C/D/I: Same as glyceryl trinitrate

P/A: 5 mg, 10 mg tablets and 20 mg sustained release capsules.

Spray: 1.25 mg released / dose, 200 metered doses.

Dose: 10 mg - 30 mg three times a day. Use eccentric dosage schedule ie instead of regular eight hourly dosage. 3 doses are given at 7 am, 11 am, 4 pm from 4 pm to 7 am no drug is administered so that a drug free interval of 15 h is produced.

Cost: Tab 10 mg (100) Rs. 10.00 - 12.00

Cap 20 mg (25) Rs. 60.00 - 62.00

Spray 200 metered doses Rs. 160.00 (1.25 mg released / dose)

Isosorbide 5 mononitrate ♦

This is an antianginal drug, which is used also in treatment of heart

5 : Drugs used in Cardiovascular Disorders

failure. The nitrates are metabolised to mononitrate in the liver. The mononitrate is the metabolically active ingredient of nitrates. Hence mononitrate preparations are now available which theoretically can ensure consistent plasma levels. Tolerance is a problem with mononitrate preparations also.

I: Angina of all types, chronic heart failure

C/I: P/C: S/E: D/I: Same as for glyceryl trinitrate

P/A: Tablets 10 mg 20 mg long acting tablets 40 mg, 50 mg and 60 mg.

Dose: Oral: 10 mg to 40 mg b.d. Long acting preparations are used once daily, eccentric dosage schedule prevents nitrate tolerance by producing nitrate free intervals of 12 h.

Cost: Tabs 60 mg (10) Rs. 35.00 - 39.00

Note on Intravenous nitroglycerine

I: Intravenous nitroglycerin is now being routinely used in coronary care units for acute myocardial infarction and other unstable ischemic syndromes. Unstable angina, refractory angina, coronary artery spasm, pulmonary oedema following LVF, infarct limitation, intra operative hypertension.

C/I: Increased intracranial pressure, hypovolemia, cardiac tamponade, obstructive lesions like aortic stenosis, mitral stenosis, hypertrophic cardiomyopathy, right ventricular infarction and glaucoma.

P/A: The drug is diluted in normal saline (5 mg - in 500 mL) and administered as a constant infusion.

It should be started at a small dose at 5 mcg/kg/min and increased gradually to achieve the desired clinical response. It can cause marked hypotension and hence blood pressure should be monitored every 15 min initially. The systemic BP should not drop more than 20 mm Hg. If the BP is less than 100 mm Hg the infusion has to be stopped or reduced temporarily. Use of plastic i.v. infusion sets may reduce the availability of nitroglycerine since it adheres to the i.v. tubing. Methaemoglobinemia may occur on continuous infusion.

Cost: Inj 5mg (5 mL) Rs 46.00

5.2.2 Miscellaneous drugs used in treatment of angina

Trimetazidine

It is an antianginal agent which acts by vasodilation and effects on cardiac metabolism.

I: Angina pectoris and myocardial infarction. At present it is mainly used in refractory angina.

C/I: Hypersensitivity

P/C: Pregnancy.

S/E: GI disturbances, vomiting, nausea.

P/A: Tablet 20 mg

Dose: 20 mg tablets t.d.s.

Mainly used at present in refractory angina.

D/I: No significant drug interaction reported.

Cost: Tab 20 mg. (10) Rs. 95.00 - 96.00

Nicorandil

I: It is a potassium channel activator and dilates arterial and venous beds. Antianginal drug for refractory angina.

C/I: Cardiogenic shock, hypotension.

P/C: Hypovolemia, pregnancy, breast feeding.

S/E: Headache, flushing, dizziness similar to that of nitrates.

P/A: Tablet 5 mg, 10 mg.

Dose: 5 mg tablets b.d. (10 mg / 24 h) the dose may be increased upto 30 mg b.d.

D/I: With alcohol and other vasodilators hypotensive action.

Cost: Tab 5 mg (20) Rs. 99.00 - 138.00

5.3 DRUGS USED FOR THROMBOLYTIC THERAPY

Major current indication for thrombolytic drugs is in acute myocardial infarction (MI) preferably within 12 hours of onset of symptoms. Thrombolytic therapy does not require an ICCU setting for its administration. Since early clot lysis is the single most effective therapeutic tool which reduces mortality and morbidity it should be the aim of the first contact physician to administer it whenever indicated.

Other indications

Pulmonary embolism, thrombosed arteries, venous shunts and prosthetic valves.

Currently available thrombolytic drugs in India include:

1. Streptokinase,
2. Urokinase
3. Tissue plasminogen activator tPA (r tPA).

Mechanism of action

The thrombolytic drugs act by converting plasminogen to plasmin. Plasmin is fibrinolytic and acts on the formed clot resulting in clot lysis. The agents which are less clot specific like streptokinase and urokinase can theoretically produce generalized fibrinolysis and a bleeding state.

Streptokinase ☆

Fibrinolytic drug

- I: Acute myocardial infarction, pulmonary embolism, thrombosed arteriovenous shunts, prosthetic valve thrombosis, peripheral arterial embolism.

5 : Drugs used in Cardiovascular Disorders

C/I: Recent hemorrhage, CVA within 1 year. Blood dyscrasias with bleeding, recent surgery, peptic ulcer, bleeding hemorrhoids, variceal bleeding, aortic dissection.

P/C: Use puncture sites (arterial and venous) which are compressible. After recent streptococcal infections, efficacy of the drug is less. Do not repeat in MI occurring 1 week - 1 year after administration due to the fear of sensitization.

S/E: Allergy with anaphylaxis in severe cases. Hypotension. Bleeding from various sites especially cerebral bleeding.

P/A: Available as injections 2,50,000 iu, 7,50,000 iu, 15,00,000 iu

Dose: 1.5 million units to be administered as continuous infusion in 100 mL saline over a period of 1h in acute myocardial infarction.

Pulmonary embolism 2,50,000 units in 30 min followed by 1,00,000 units 1 h for 24 h.

D/I: Use with caution in patients already receiving anticoagulants like heparin, antiplatelet drugs such as aspirin or dipyridamol.

Special Note : Streptokinase is not at present indicated in acute MI presenting after 12 hours and also in cases with ST segment depression (except in cases of suspected true posterior MI). Can also be given upto 24 hrs if there is persistent cardiac pain. If streptokinase is repeated after 1 week to 1 year in patients who have recurrent infarction the efficacy is dampened due to the development of antibodies. In such situation alternate drugs such as urokinase or tPA are indicated.

Cost : Inj vial (1500000 iu) about Rs. 2300.00 - 3500.00

Storage : Store between 15 - 30°C

Streptokinase injection should be reconstituted prior to the use and used immediately. If it is not administered soon it should be stored at 2-8 °C.

Urokinase ✧

Fibrinolytic drug produced in the body.

I: Same as for streptokinase. Additional indication is intraocular clot lysis.

C/I: Same as for streptokinase

P/C: Bleeding from puncture site.

S/E: Being a naturally occurring substance allergic reactions are considerably less. Hypotension is less compared to streptokinase. Less sustained systemic fibrinolysis when compared to streptokinase.

P/A: Available as injections 50,000 iu, 2,50,000 iu, 5,00,000 iu, 7,50,000 iu, 10,00,000 iu.

Dose: Acute myocardial infarction. 1.5 million units in 100 mL saline to be given as infusion over 1 h. Pulmonary embolism. 4400 iu/kg over 10 min followed by 4400 iu/kg/h for 24 h.

D/I: Aspirin and indomethacin can cause haemorrhage. Heparin and oral anticoagulants will increase the risk of bleeding.

Cost: Inj vial (500000 iu) Rs. 3700.00

Storage : Store between 2- 8 °C, protect from freezing. Because urokinase injection does not contain any preservatives it should not be reconstituted until immediately prior to use.

Tissue Plasminogen Activator (Altepase) tPA

Fibrinolytic drug manufactured by recombinant DNA technology.

- I: 1. Acute myocardial infarction.
2. Prosthetic valve thrombosis.
3. Pulmonary embolism.

C/I: Same as for streptokinase.

P/C: Though, it is thought to be clot specific and less likely to cause bleeding due to fibrinolysis still bleeding complication have to be watched for.

S/E: When compared to streptokinase it produces a slight increase on the incidence of haemorrhagic stroke. Patients sensitive to gentamicin should not use tPA.

P/A: Injections 50 mg vial.

Dose: Total dose over 90 min

Initial bolus 15 mg

Intravenous infusion 50 mg over 30 min 35 mg over 60 min. Another dosage schedule is 50 mg i.v. bolus x 2 doses spaced at 3 min interval.

D/I: Increased risk of GI bleeding with NSAID's, increased risk of haemorrhage with warfarin.

Note: Due to a very short half life, tPA administration should be followed by intravenous heparin infusion to prevent arterial occlusion by further thrombosis

Cost: Inj vial (50 mg) Rs. 25,695.00

Storage : Store between 2 - 30°C. Protect from excessive exposure to light.

5.4 ANTIPLATELET DRUGS

Aspirin

- I: Coronary artery disease, cerebrovascular diseases, fever, rheumatic fever, other arthritides.

Dose: Antiplatelet dose : 75 to 150 mg daily along with food.

Dipyridamole

- I: After prosthetic valve implantation and dipyridamole stress echocardiography.

C/I: Acute myocardial infarction, severe aortic stenosis, crescendo angina.

5 : Drugs used in Cardiovascular Disorders

P/C: Rapidly worsening angina, aortic stenosis, recent myocardial infarction, may exacerbate migraine, hypotension.

S/E: Nausea, hot flushes, tachycardia, headache.

P/A: Tablets 25 mg, 75 mg, 100 mg.

Dose: 300 mg in divided doses daily.

D/I: Increases the action of adenosine and anticoagulants.

Cost: Tab 25 mg (10) Rs. 3.00 - 4.00

Ticlopidine

I: Myocardial ischemia, thromboembolic strokes, following interventions like angioplasty and stent implantation post coronary bypass surgery.

C/I: Haematological abnormalities.

P/C: GIT disturbances, neutropenia, agranulocytosis.

S/E: Neutropenia or agranulocytosis, thrombocytopenia, SLE, skin rash, gastrointestinal disturbances.

P/A: Tablets 250 mg

Dose: 250 mg b.d.

D/I: Risk of haemorrhage increased with aspirin and oral anticoagulants, increase in theophylline half life, slight reduction in digoxin plasma levels.

Cost: Tab 250 mg (10) Rs. 110.00 - 160.00

5.5 ANTICOAGULANTS

Major anticoagulant drugs are heparin and oral coagulant drugs belonging to the warfarin group and phenindione group. They are widely used in cardiology for various indications.

(see also anticoagulants in haematology - section 9.10)

Coronary artery disease

- Unstable angina.
- Acute infarction.
- LV thrombus.

5.5.1 Systemic anticoagulants

Heparin ✧

Anticoagulant drug for parenteral use.

I: Dilated cardiomyopathy, valvular heart disease, pulmonary embolism, atrial fibrillation, deep vein thrombosis, patients requiring cardioversion.

C/I: Haemophilia and other bleeding disorders, thrombocytopenia, peptic ulcer, severe liver diseases, recent CVA, recent surgery, recent trauma.

P/C: Can induce thrombocytopenia, careful use in renal and hepatic diseases.

S/E: Haemorrhage, thrombocytopenia, hypersensitivity reactions, osteoporosis after prolonged use, alopecia

P/A: Injections 20,000 iu, 5000 iu, 25,000 iu

Dose: Myocardial infarction, pulmonary embolism, deep vein thrombosis 5000 units i.v. bolus followed by continuous infusion of 1000 units hrly for 24 h.

Subcutaneous heparin 7500 - 12500 units b.d.

Low dose heparin 1500 units subcutaneously is given prophylactically to prevent venous thrombosis.

D/I: Aspirin enhances the anticoagulant effect of heparin, NSAIDs should be used with caution because of the risk of gastro intestinal bleeding. Dipyridamole also increases the anticoagulant effect.

Note: *Overdose of heparin is treated by protamine administration. Dose of heparin should be adjusted depending on the partial thromboplastin time, the patients value should be 1 ½ - 2 times the control value.*

Cost: Inj 5000 iu/mL (5 mL) Rs. 68.00 - 69.00

Low molecular weight heparin

A variety of preparations are available and have the same indications that conventional heparin has:

- a. Dalteparine sodium fragmine 5000 units.
- b. Tinzaparine
- c. Enoxaparine
- d. Nadroparine (fraxiparine)
- e. Parnaparine (fluxum)

5.5.2 Oral anticoagulants

I: Deep vein thrombosis, pulmonary embolism, atrial fibrillation in mitral valve disease, dilated cardiomyopathy, LV thrombus following myocardial infarction, and prosthetic valves.

C/I: Early pregnancy and active bleeding states.

Dose: The administration of oral anticoagulants is adjusted according to the prothrombin time. The overdose of oral anticoagulants can be treated by administration of vitamin K.

Warfarin ♦

I: Deep vein thrombosis, prosthetic valves, atrial fibrillation, pulmonary embolism, LV thrombus.

C/I: Pregnancy, bleeding disorders, bacterial endocarditis.

5 : Drugs used in Cardiovascular Disorders

P/C: Recent surgery, hepatic disease, renal disease.

S/E: Haemorrhage.

P/A: Tablets 5 mg.

Dose: Loading dose 10 mg for 2 days then adjust dose, according to prothrombin time (INR 1.5 - times control). In cases of prosthetic valves, the INR should be kept at 3 - 4.5. Patients should be instructed regarding bleeding complications when they are on warfarin.

D/I: Alcohol, anabolic steroids, amiodarone, ciprofloxacin, erythromycin, antiplatelet drugs, simvastatin, thyroxine, all increase the anticoagulant effect. Vitamin K barbiturates, cisapride, reduce the effect of anticoagulants.

Cost: Tab 5 mg (10) Rs. 18.00 - 19.00

Acenocoumarol

I, C/I, P/C, D/I: Same as warfarin

S/E: Agranulocytosis, allergic dermatitis, diarrhoea, sores, ulcers, loss of appetite, unusual hair loss.

P/A: Tablets 1 mg, 2 mg, 4 mg

Dose: 8 mg first day, 4-8 mg second day, maintenance dose 1-8 mg daily depending on the prothrombin time.

Cost: Tab 2 mg (10) Rs. 29.00 - 30.00

Phenindione

I, C/I, P/C, S/E, D/I: Same as warfarin

P/A: Tablets 50 mg.

: 200 mg first day, 100 mg second day, maintenance 50 - 100 mg daily depending on the prothrombin time.

Cost: Tab 50 mg (100) Rs. 100.00 - 101.00

5.6 LIPID LOWERING DRUGS

Lipid Lowering drugs are used in hyperlipidemia. The major groups of drugs used are the anion exchange resins, fibric acid derivatives, HMG CoA reductase inhibitors (statins) nicotinic acid and fish oils. But the drugs that are available to us are few and includes the statins, fibrates and nicotinic acid. These drugs are differing in their mode of action and different drugs are used in different hyperlipidemic states.

5.6.1 Statins

Mechanism of action is by inhibiting the enzyme HMG CoA reductase which is involved in endogenous cholesterol synthesis. These drugs are useful in lowering of total cholesterol and LDL cholesterol, but are less useful in

hypertriglyceridemia. Statins can reverse the already established atheromatous lesion in the coronary artery.

Lovastatin

I: Hypercholesterolemia, mixed hyperlipidemia.

C/I: Active liver diseases, pregnancy, breast feeding.

P/C: Hepatic diseases, high alcohol intake.

S/E: Reversible myositis, headache, altered hepatic enzymes, abdominal pain, nausea.

P/A: Tablets 10 mg, 20 mg.

Dose: 20-40 mg to be given after dinner h.s.

D/I: Increased action with anti coagulants, increased incidence of myopathy with fibric acid derivatives and cyclosporine.

Cost: Tab 20 mg (10) Rs. 80.00 - 125.00

Simvastatin

I, C/I, P/C, S/E, D/I: Same as lovastatin

P/A: Tablets 5 mg, 10 mg, 20 mg.

Dose: 10 mg at h.s.

Cost: Tab 10 mg (10) Rs. 80.00 - 81.00

Other drugs in this class are pravastatin, atorvastatin, fluvastatin. These are not freely available in India at present.

5.6.2 Fibric acid derivatives

These are mainly used in the treatment of hypertriglyceridemia though they also reduce LDL cholesterol and increase HDL cholesterol to a small degree. The earliest drug in use was clofibrate which is not used nowadays. The commonly used drugs in this group are gemfibrosil and bezafibrate.

Gemfibrosil

I: Hyperlipidemias type 2a, 2b, 3, 4, 5

C/I: Alcoholism, pregnancy, breast feeding, active liver disease, cholecystitis.

P/C: Myositis like syndrome, renal dysfunction, hepatic dysfunction.

S/E: Nausea, vomiting, diarrhoea, dermatitis, angioedema, myopathy, myasthenia, cholestatic jaundice.

P/A: Capsules 300 mg, 600 mg

Dose: 600 mg b.d.

D/I: Increases the effect of anticoagulants. Increase the myopathic effect of statins.

Cost: Cap 300 mg (10) Rs. 70.00 - 100.00

Bezafibrate

I, C/I, P/C :S/E, D/I: Same as gemfibrosil

P/A: Tablets 200 mg, 400 mg

Dose: 200 mg t.d.s.

Cost: Tab 200 mg (10) Rs. 77.00 - 78.00

5.6.3 Nicotinic Acid

Dose: 100 mg t.d.s. for indefinite period.

5.7 ANTIHYPERTENSIVE DRUGS

Hypertension is a common disease affecting approximately 25% of the adult population. In adults blood pressure above 140/90 mm Hg qualify to be considered hypertensive demanding treatment. The treatment measures may be non-pharmacological such as rest, exercise, diet, etc. or drug therapy. Ideal hypertensive drug should have the following properties.

- a. Predictable efficacy to reduce BP.
- b. Rapid onset and sustained action.
- c. Should not damage the renal or hepatic system.
- d. There should not be tolerance and should not cause drug interaction with other drugs.
- e. Should be cheap.

There is no drug available at present satisfying all these criteria. It is to be noted that isolated systolic hypertension also demands therapy.

5.7.1 Classification of antihypertensive drugs.

1. Diuretics.
2. Beta - adrenergic blockers.
3. Calcium channel blockers.
4. Vasodilators - diazoxide, hydralazine, minoxidil, nitroprusside.
5. Centrally acting agents - clonidine, guanabenz, methyldopa, reserpine.
6. Alpha - adreno receptor blocking agents - indoramin, phenoxybenzamine, phentolamine, prazosin.
7. Adrenergic neuron blocking agents - bethanidine, debrisoquine, guanethidine.
8. ACE inhibitor - captopril, enalapril.
9. Ganglion blocking agents - pentolinuine, trimetaphan.

10. Angiotension II Receptor antagonists - losartan.
11. Miscellaneous
 - a. Rauwolfia alkaloid - reserpine.
 - b. MAO inhibitor - pargyline.
 - c. Serotonin blocking agent - ketanserin.

5.7.2 Diuretics

They are mainly used for treatment of oedematous states. They lead to renal excretion of sodium, potassium and water in varying proportions. They are indicated in fluid overload situations such as congestive heart failure, nephrotic syndrome, cirrhosis of liver and others. They lower blood pressure and therefore they are employed either as primary or as adjuvant drugs in the treatment of hypertension.

Commonly used diuretics are:

- Thiazide diuretics
- Loop diuretics
- Potassium sparing diuretics.
- Osmotic diuretics.
- Carbonic anhydrase Inhibitors.

5.7.2.1 Thiazide diuretics

Hydrochlorothiazide ☆

- I: Congestive cardiac failure, renal oedema, ascites, systemic hypertension.

Dose: 25 - 100 mg daily.

Chlorthalidone ☆

I, C/I, P/C, S/E, D/I: Similar to hydrochlorothiazide but longer duration of action.

Dose: 50 - 100 mg daily.

Note: It is better to supplement oral potassium in doses of 1-2 g b.d. or t.d.s. along with thiazides and loop diuretics.

Indapamide

This is a weak diuretic. It potentiates the action of other standard antihypertensive drugs

- I: Systemic hypertension

Dose: 2.5 mg daily for systemic hypertension.

Xipamide

- I: Systemic hypertension, mild to moderate oedema.

Dose: Oral oedema due to a variety of causes; start with 40mg/day

5 : Drugs used in Cardiovascular Disorders

reducing to 20 mg /day according to patient response.

Hypertension : 20 mg daily as a single dose.

5.7.2.2 Loop Diuretics

Compared to thiazide diuretics, loop diuretics are more potent. They also process vasodilator property. They are more effective in the management of oedematous states and acute pulmonary oedema but are not suitable drugs for systemic hypertension, where a less potent but more prolonged diuretic action such as that of thiazides is more advantageous.

The loop diuretics act at the loop of Henle inhibiting $\text{Na}^+ / \text{K}^+ / \text{Cl}^-$ transport.

Frusemide (furosemide) ✧

This is the most common loop diuretic currently in use.

I: Oedematous states, oliguria due to acute renal failure, acute pulmonary oedema in systemic hypertension.

Dose : Oral : 40 to 80 mg daily in severe cases, upto 100 mg/day in divided doses can be given.

Parenteral: Intravenous frusemide 40 - 80 mg i.v. can be given in acute situation as bolus dose. Much higher dose of the order of 250 - 1000 mg can be given i.v. as infusion in circumstances where acute oliguric renal failure is impending.

Note: It is better to use frusemide in oedema states and thiazide diuretics in systemic hypertension. For acute oliguric renal failure and to prevent impending anuria, vials containing larger doses upto 500mg are available.

Bumetanide

I, C/I, P/C, S/E, D/I: Similar to frusemide.

Dose: 1 - 2 mg per day in single or divided doses.

Ethacrynic acid

I, C/I, P/C, S/E, D/I : Similar to frusemide.

Dose: 50 - 100 mg daily.

5.7.2.3 Potassium Sparing Diuretics

Major adverse side effects of thiazides and loop diuretics is hypokalemia. Potassium sparing diuretics do not cause hypokalemia and therefore they can be given singly or in combination with thiazides or loop diuretics. Their clinical effectiveness as diuretics is considerably less in comparison to frusemide.

Potassium sparing diuretics are

1. Aldosterone antagonists, spironolactone.
2. Amiloride.
3. Triamterene.

Spirolactone ✧

This potassium sparing diuretic is a competitive inhibitor of aldosterone.

- I: Weak diuretic used in cirrhosis, nephrotic syndrome and primary hyperaldosteronism in which it is the drug of choice. Also used along with thiazide and loop diuretics to counteract the loss of potassium.

Dose: 25 mg 6 h upto 100 mg/day

This dose may be increased upto 400 mg / day in divided doses in selected cases.

Triamterene

- I: It is indicated in oedematous states, in combination with thiazides or loop diuretics. When potassium loss is to be minimized. Uncontrolled use may lead to hyperkalemia.

Dose: 150 - 250 mg daily 50 mg in combination with thiazides.

Amiloride

This is a potassium sparing diuretic used in combination with loop diuretics or thiazide.

- I: Oedematous states especially in prolonged administration.

Dose: 5 mg - 10 mg / day.

5.7.3 Beta (β) Adrenergic Blockers

Since their introduction in 1964 beta blockers has become a very important group of drugs used in cardiovascular disease in the treatment of hypertension coronary artery disease and cardiac arrhythmias.

Beta blockers act in the beta receptors present in the heart, blood vessels, kidney, liver and bronchii. The different preparations have different action predominantly and therefore one particular drug may be more effective in one indication compared to another. Beta receptors are divided into β_1 and β_2 receptors. β_1 receptors are present in the heart, kidney, adipose tissue and to some extent in the bronchus. β_2 receptors are present in the bronchus, vascular smooth muscle, GIT, uterus, pancreas and coronary arteries. The ratio of β_1 and β_2 receptors in the heart is 70 : 30.

Mechanism of action:

In the heart beta blockers reduce the heart rate, decrease in myocardial contractility and velocity of cardiac contraction. These effects produce a decrease in the myocardial oxygen demand, which is the most important effect in the reduction of angina. In the conducting system of heart, these drugs affect the phase 4 of the action potential (diastolic depolarisation) and also suppress catecholamine mediated cardiac arrhythmias. Beta blockers reduce renin release from the juxtaglomerular cells. They also reduce the sympathetic vasoconstrictor effect in the blood vessels thus reducing the peripheral resistance and carry reduction in blood pressure.

Beta blockers have different properties.

5 : Drugs used in Cardiovascular Disorders

1. Cardioselectivity (atenolol, metoprolol, esmolol, bisoprolol, acebutalol)
2. Intrinsic sympathomimetic activity, (acebutalol, pindolol)
3. Hydrophilicity (atenolol, nadolol, sotalol)
4. Membrane stability effect (propranolol)
5. Vasodilator property. (carvedilol, celiprolol)

Each beta blockers has variability in these properties and hence in different clinical situation one betablocker may be superior to another.

Indication for Beta blockers

Systemic hypertension, coronary artery disease - (acute myocardial infarction, effort angina), hyper trophic cardiomyopathy, cardiacarrhythmias (ventricular, supraventricular), thyrotoxicoses, glaucoma, migraine, selected cases of heart failure, Marfans syndrome, portal hypertension, cyanotic congenital heart disease with apnoeic spells.

Propranolol ✧

Antianginal, antihypertensive, antiarrhythmia,

- I: Systemic hypertension, coronary artery disease, effort angina, supraventricular tachyarrhythmias, ventricular arrhythmias, migraine, thyrotoxicosis, hypertrophic cardiomyopathy, congenital cyanotic heart disease with spells.

C/I: AV Blocks, sick sinus syndrome, overt CHF, peripheral vascular disease, asthma.

P/C: Early congestive cardiac failure, vasospastic angina, peripheral vascular disease, myasthenia gravis, bradycardia, chronic obstructive airway disease, diabetes mellitus, pregnancy, lactation, Raynaud's disease should not be used alone in phaeochromocytoma.

S/E: Bradycardia, cold extremities, gastrointestinal upset, fatigue, conduction disorders.

P/A: Tablets 10 mg, 40 mg, 80 mg

Sustained release capsules 40 mg, 80 mg.

Dose : Hypertension : 40 mg b.d. or t.d.s. Maximum dose 160 mg - 320 mg daily.

Angina : 40 mg b.d. or t.d.s. Maintenance 120 - 240 mg dose

Arrhythmias, anxiety, tachycardia: 10 - 40 mg t.d.s.

Post MI Secondary prophylaxis : 40 mg t.d.s. 5 days after MI - for secondary prophylaxis. For i.v. injection in arrhythmias give 1 mg over 1 min.

D/I: Use with caution when patient is on verapamil or diltiazem since the risk of increase in AV block and worsening of heart failure exist. Intravenous verapamil or diltiazem should not be given in patients receiving betablockers. Betablocker mask cardiovascular symptoms of hypoglycemia when used with oral hypoglycemics -

hence hypoglycemia may go unrecognised, may worsen bradycardia when used with digoxin, antihypertensive effect is potentiated with diuretics.

Note : The dose requirement of beta blockers in Indian population is usually less than that of the Western population. It is better to start with smaller doses.

Cost:Tab 10 mg (10) Rs. 4.00 - 5.00

Sotalol

I: It is a non selective beta blockers with the class III antiarrhythmic property. Ventricular arrhythmias and supraventricular arrhythmias, systemic hypertension, angina, thyrotoxicosis.

C/I, P/C, S/E, D/I: Same as propranolol.

P/A: Tablets 40 mg and 80 mg .

Dose : Oral : For hypertension and angina, initially 80 mg b.d. or 160 mg daily; maintenance dose is 160 mg daily, increased to 400- 600mg daily if necessary. Arrhythmias, 120 -240 mg daily in single or divided doses.

Thyrotoxicosis: 120-240 mg daily in single or divided doses

Prophylaxis after infarction: 320 mg daily, starting 5-14 days after infarction.

By slow i.v. 20-60 mg over 2-3 min with ECG monitoring. It is repeated if necessary with 10 min intervals between injections, upto a total dose of 100mg the injection being given in 3 min.

Note: Excessive bradycardia can be countered with i.v. atropine 0.6-2.4 mg in divided doses of 600 mcg each time.

Cost:Tab 40 mg (10) Rs. 12.00 - 13.00

5.7.3.1 Cardio selective betablockers

Metoprolol

I, C/I, P/C, S/E, D/I: Same as propranolol

P/A: Tablets 50 mg 100 mg, 200 mg (long acting)

Injection 1 mg/ mL.

Dose : In hypertension - 50 mg b.d. increase to 200 mg daily in divided dose.

In angina 50 mg -100 mg b.d. - t.d.s.

Arrhythmias 50 mg b.d. - t.d.s.

In acute myocardial infarction i.v. metoprolol given at a dose of 5 mg at 5 min. intervals for 3 doses upto a maximum of 15 mg with in the first 6 hours has been shown to reduce the mortality in patients who have no contraindication to beta blockade therapy.

Cost:Tab 50 mg (10) Rs. 82.00 - 83.00

Atenolol ☆

I, C/I, P/C, S/E, D/I: Same as propranolol.

P/A: Tablets 25 mg, 50 mg, 100 mg.

Injection 500 mcg / mL.

Dose: Hypertension 50 mg daily increase upto 100 mg

Effort angina 50 - 100 mg daily.

Arrhythmias 50 - 100 mg daily.

In the absence of contraindication, in post MI cases atenolol given in dose of 5 mg i.v. slowly helps to reduce arrhythmias and episodes of sudden death.

Note: Being water soluble, it does not cross blood - brain barrier. Therefore fatigue, nightmares and other CNS side effects are less.

Cost: Tab 50 mg (14) Rs. 19.00 - 31.00

Bisoprolol

I: Hypertension, angina

C/I, P/C, S/E, D/I: Same as propranolol.

P/A: Tablet 5 mg

Dose: 5 mg daily.

Cost: Tab 5 mg (10) Rs. 82.00 - 83.00

Esmolol

Ultra short-acting betablocker for parenteral use, with a half life of 9 min.

I: Supra ventricular arrhythmias, peroperative hypertension, tachycardia.

C/I: Severe hypotension, asthma, severe COPD, other contraindication for betablockers use.

P/C: Hypotension, diabetes mellitus, renal impairment, pregnancy

S/E: Confusion, redness or swelling at the site of injection, reduction in peripheral circulation.

P/A: Injection 10 mL ampoule each mL contains 100 mg.

Dose: S.V.T 500 mcg / kg/ min for 4 min.

Maintenance dose is 150 - 300 mcg/kg/min.

D/I: Concurrent use of phenytoin with i.v. esmalol produces additive cardiac depressant effect, increases the risk of bradycardia, AV block, hypotension. When given along with calcium channel blockers i.v. cardiac failure may be precipitated. Esmalol may increase blood digoxin levels.

Cost: Inj 100 mg/10 mL (10 mL) Rs. 48.00 - 50.00

5.7.3.2 Drugs with combined alpha and beta blocker effect

Labetalol

I: Systemic hypertension, hypertensive emergencies, phaeochromocytoma.

C/I: AV Block, bronchospasm, cardiogenic shock.

P/C: CHF, diabetes mellitus, liver dysfunction, postural hypotension.

S/E: Headache, hallucination, impotence.

P/A: Tablets. 50 mg, 100 mg, 200 mg.

Dose: 50 mg b.d., increased to 100 - 200 mg b.d.

D/I: Cimetidine increases bioavailability of labetalol, action of oral hypoglycemic agents increased, with anaesthetic agents may cause myocardial depression.

Cost: Tab 50 mg (10) Rs. 15.00 - 16.00

Carvedilol

Carvedilol is a beta blocker with additional vasodilatory action. Therefore it lowers peripheral resistance also.

I: Hypertension and in patients with mild CHF

C/I, P/C: Same as propranolol

S/E: postural hypotension, headache, fatigue, flu-like symptoms, rarely angina, heart block, allergic skin rashes, nasorespiratory allergy, mental depression, insomnia, paresthesia, hepatic dysfunction, leucopenia, thrombocytopenia.

P/A: Tablets 12.5 mg, 25 mg

Dose: Start with 6.25 mg daily orally and increased to 25-50 mg depending upon clinical response. Lower dose in elderly patients(25 mg)

Cost: Tab 12.5 mg (10) Rs. 95.00-100.00

5.7.4 Calcium channel blockers

These drugs affect the slow calcium channel and prevent the inward movement of calcium into the cells. Sites of action include myocardial cell, conduction tissue and vascular smooth muscles. The different drugs vary in their efficacy of action at different sites. All these drugs impair the force of contraction of myocardium and should be avoided in heart failure. Main indications are the treatment of systemic hypertension, angina, supraventricular arrhythmias, hypertrophic cardiomyopathy and cerebrovascular diseases. Different drugs have different preferential action and indication and hence each drug has to be used for specific clinical indication.

Verapamil ♦

This is a calcium channel blocker drug with antihypertensive, antianginal and antiarrhythmic properties.

1. Supraventricular tachycardias, systemic hypertension, coronary artery disease with effort angina and vasospastic angina, hypertrophic cardiomyopathy, migraine.

C/I: Congestive heart failure, AV block, sinus node dysfunction, hypotension, atrial fibrillation and atrial flutter in WPW syndrome.

5 : Drugs used in Cardiovascular Disorders

porphyria. Intravenous verapamil should not be given to patients receiving parenteral or oral beta blockers due to the risk of development of cardiac asystole.

- P/C: Hepatic disease, pregnancy, breast feeding, concomitant administration of beta blockers (oral).
- S/E: Most important and frequent side effect is constipation. Others include headache, dizziness, ankle oedema, allergic reaction, nausea, vomiting, flushing.
- P/A: Tablets - 40 mg, 80 mg, 120 mg 240 mg sustained release form.
Injections 5 mg in 2 mL.
- Dose: 120 mg - 240 mg daily in divided dosage or sustained release form.
Intravenous dosage. 2.5 - 5 mg. Slow i.v. bolus up to 10 mg.
- D/I: Increased risk of bradycardia and AV block with betablockers. Serum digoxin levels may increase, risk of bradycardia with amiodarone, negative inotropism with disopyramide.
- Cost:

Tab	40 mg	(10)	Rs. 5.00 - 10.00
Inj	5 mg/ 2 mL	(2 mL)	Rs. 3.00 - 4.00

Diltiazem ✧

Antianginal, antiarrhythmic and antihypertensive.

- I: All types of angina non - Q wave myocardial infarction, supraventricular tachycardia, systemic hypertension.
- C/I: In left ventricular failure, AV block, sick sinus syndrome, pregnancy.
- P/C: Hepatic and renal impairment, LV dysfunction, first degree heart block.
- S/E: Constipation, ankle oedema, hepatitis, manic depression, rashes, hypotension.
- P/A: Tablets 30 mg, 60 mg, 90 mg, 120 mg sustained release.
Injection 5 mg/mL (5 mL)
- Dose: 90 - 180 mg orally daily in divided doses to start with. This may be increased to 360 mg/day in severe cases.
Parenteral: To be administered as slow i.v. 0.25 mg/kg or as a bolus of 10 - 12.5 mg for supraventricular tachycardias.
- D/I: Same as verapamil.
- Cost:

Tab	30 mg	(10)	Rs. 18.00 - 19.00
Inj	5 mg/mL	(5 mL)	Rs. 17.00 - 20.00

Nifedipine ✧

This has antihypertensive, antianginal properties, when given sublingually it leads to rapid fall of blood pressure.

- I: Systemic hypertension, angina, Raynauds phenomenon.

- C/I: Severe aortic stenosis, severe hypotension including cardiogenic shock.
- P/C: May worsen angina if used alone in some patients. This drug should not be used as monotherapy in patients after MI and unstable angina due to risk of higher mortality. In pregnant women it may cause inhibition of labour. Though negative inotropic effect is only slight, it should be used with caution in patients with heart failure.
- S/E: Headache, nausea, flushing, tachycardia, pedal / ankle oedema, constipation, gingival hyperplasia.
- P/A: Capsules and tablets - 5 mg, 10 mg, 20 mg retard tablets.
- Dose: 30 mg o.d. single dose.
30 mg GITS (Gastro intestinal delivery system).
- It is now considered prudent not to use small and frequent dose of nifedipine but to use sustained release form.
- D/I: Nifedipine may reduce quinidine levels, it may interact with prazosin and cause severe hypotension. Hepatic metabolism of nifedipine may be affected by ranitidine or cimetidine.
- Note: *Nifedipine when given sublingual causes rapid fall of blood pressure, in hypertensive emergencies. Since this may lead to cerebrovascular insufficiency this route of administration should be used with caution.*
- Cost: Cap 10 mg (10) Rs. 6.00 - 20.00
SR Tab 20 mg (10) Rs. 10.00

Amlodipine ✧

This calcium channel blocker has longer duration of action as an antihypertensive and antianginal drugs. The half life is 36 h and so the duration of action is long and the effect is sustained.

- I: Systemic hypertension, all types of angina pectoris.
- C/I: Severe aortic stenosis.
Systemic hypotension.
- P/C: Use with caution in the elderly as its long duration of action may produce long periods of hypotension. Use with caution in hepatic dysfunction, pregnancy, lactation and fever.
- S/E: Pedal oedema, ankle oedema, constipation, nausea, flushing, hyperplasia of gums.
- P/A: Tablets / capsules 2.5 mg, 5 mg, 10 mg
- Dose: 2.5 - 10 mg daily as single dose.
- D/I: It has common drug interaction as with other dihydropyridines. It has beneficial effect in angina if combined with beta blockers
- Cost: Tab 5 mg (10) Rs. 5.00 - 30.00

Felodipine

Anti hypertensive, antianginal calcium blocker.

- I: Systemic hypertension, angina

5 : Drugs used in Cardiovascular Disorders

C/I, P/C, S/E, D/I : Similar to other dihydropyridines.

P/A: Tablets 2.5 mg, 5 mg, 10 mg.

Dose : Start with 2.5 - 5 mg daily as tablets or capsules and increase according to response upto a maximum dose of 20 mg daily

Cost: Tab 2.5 mg (10) Rs. 18.00 - 22.00

Nimodipine

Calcium channel blocker with particular effect in improving cerebral circulation.

I: Cerebro vascular arterial spasm following subarachnoid hemorrhage.

C/I: Hypersensitivity, hypotension, lactation.

P/C: Raised intracranial pressure.

S/E: Hypotension, flushing, headache, nausea.

P/A: Tablet - 30 mg,

Capsule - 30 mg,

Injection i.v. 50 mL vial.

Dose : 1 mg/hour initially as a infusion and increased to 2 mg/hour after 2 hours.

After subarachnoid haemorrhage to prevent neurological defecits and continue for 21 days orally 60 mg x 4 h for 4 days

Mainly these are indicated in hypertension.

D/I: Same as other dihydropyridine groups.

Cost: Tab 30 mg (10) Rs. 50.00 - 60.00.

Inj iv 50 mL (vial) Rs. 105.00.

Other dihydropyridine drugs available in India include

1. Nitrendipine
2. Lacidipine

5.7.5 Vasodilator drugs

Diazoxide

I: Hypertensive emergencies, hypoglycemia.

C/I: Dissection of aorta, hypertensive crisis with acute LVF (marked retention of sodium and water)

P/C: Hyperuricemia, diabetes, ischaemic heart disease, pregnancy, lactation.

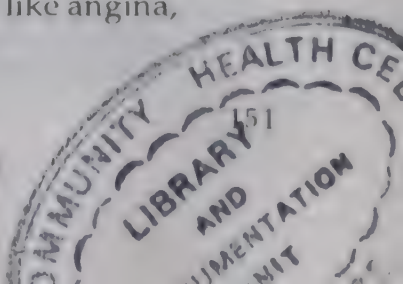
S/E: Tachycardia, hyperglycemia, salt and water retention.

P/A: Injection 15 mg/mL

Dose : 50 - 150 mg i.v. bolus rapidly into or peripheral vein. Earlier dose of 300 mg i.v. associated with side effects like angina, cerebral infarction.

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Note : With the availability of newer drugs with little side effects like nitroprusside and nitroglycerine, diazoxide is not currently used for hypertensive emergencies.

Hydralazine

- I: Hypertension, parenteral use in hypertensive crisis.
- C/I: Dissecting aortic aneurysm, mechanical obstructive lesions like aortic stenosis, mitral stenosis.
- P/C: May cause angina in ischaemic heart disease. Use with caution in lactating mothers.
- S/E: Lupus erythematosus like syndrome, tachycardia, fluid retention, headache, rashes, peripheral neuropathy.
- P/A: Tablets 25 mg
- Dose: Tablets 25 mg b.d., increase upto 50 mg b.d.
Slow i.v. injection 5 - 10 mg over 20 min. May be repeated after 30 min.
- Note : Hydralazine is not freely available at present, but has been favoured in the treatment of pregnancy induced hypertension earlier along with alpha methyl dopa.*
- Cost : Not freely available.

Minoxidil

- I: Systemic hypertension, male pattern baldness.
- C/I: Pheochromocytoma.
- P/C: Angina, pregnancy, porphyria.
- S/E: Salt and water retention, tachycardia, increased hair growth, rashes, nausea, vomiting.
- P/A: Tablet 2.5 mg
Solution 20 mg/mL
- Dose: Tablets 5 mg o.d. in divided doses. Gradually increase to 50 mg o.d.
- D/I: Potentiation of hypotensive effect with neuroleptics.
- Cost: Tablet not freely available
Solution 20 mg/mL (60 mL) Rs. 133.00 - 202.00

Sodium Nitroprusside

- I: Hypersensitive crisis, to control blood pressure during anaesthesia, acute heart failure.
- C/I: Hepatic dysfunction, abnormalities of cyanide metabolism. Lebers optic atrophy, tobacco amblyopia, Vitamin B12 deficiency.
- P/C: Severe renal insufficiency, hypothyroidism, impaired cerebral circulation, elderly patients, hypothermia.
- S/E: Tachycardia, dizziness (due to rapid fall in BP) abdominal pain, nausea, palpitation, retrosternal discomfort, cyanide toxicity

5 : Drugs used in Cardiovascular Disorders

P/A : Injection 50 mg/mL

Dose : 0.5 mg/kg/min to begin with increase gradually every 5 min till the desired reduction is obtained. Average dose is 3 mg/kg/min.

D/I : Sensitivity enhanced by antihypertensives. Combination therapy with diuretics and inotropic agents are useful in cardiac failure.

Note : Sodium nitroprusside is currently a very popular drug in producing controlled hypotension. The intravenous line should be protected from sunlight to prevent loss of efficacy.

Cost : Injection 50 mg/mL (5 mL) Rs. 45.00 - 130.00

5.7.6 Centrally acting antihypertensive drugs

Major drugs in this group are clonidine and alpha methyl dopa.

Clonidine

Antihypertensive action is by inhibiting sympathetic outflow from CNS.

I : Systemic hypertension. It is not recommended as the first line drug.

C/I : Depression

P/C : Sudden cessation of treatment with clonidine causes rebound hypertension. Use with caution in Raynaud's syndrome, occlusive arterial disease and renal disease.

S/E : Sedation, dry mouth, fluid retention, Raynauds phenomenon, headache, dizziness, constipation bradycardia

P/A : Tablets 0.1 mg (100 mcg), 0.15 mg (150 mcg).

Dose 0.05-0.1 mg in divided doses.

D/I : Tricyclic antidepressants decrease the effect of clonidine. Beta blockers administration also not advocated concomitantly as risk of withdrawal hypertension is markedly increased. Also to be avoided if MAO inhibitors are used.

Note : Use in resistant case or where other antihypertensive drugs are contraindicated. Can be used in renal dysfunction and effective in controlling hypertensive crisis.

Cost: Tab 100 mcg (10) Rs. 5.00 - 6.00

Alpha Methyldopa ☆

I : Systemic hypertension. This drug is especially safe in pregnancy induced hypertension.

C/I : Active liver disease, depression, phaeochromocytoma, porphyria.

P/C : May cause positive coombs test, sedation often troublesome.

S/E : Dry mouth, diarrhoea, fluid retention, haemolytic anaemia, giddiness due to postural hypotension, sexual impotence.

P/A : Tablet 250 mg

Dose : Start with 250 mg b.d. and gradually increase depending on response upto 3 g/day.

D/I: Enhanced hypotensive effect with alcohol, anaesthetics, anti-depressants, other anti-hypertensives, anti-psychotics, beta blockers, calcium channel blockers, diuretics and nitrates. Carbenexolone antagonizes hypotensive effect.

Note : *It is better to continue alpha methyl dopa with a diuretic as the combination is more effective and decreases the fluid retention caused by alpha methyl dopa. Drugs acting on autonomic ganglia like hexamethonium, pentolinium, mecamlamine, trimetaphan and pempidine are not currently used in the treatment of hypertension due to the availability of better and less toxic newer drugs. Drugs acting in post ganglionic sympathetic nerve endings include the adrenergic neurone blockers - guanethidine, bethanidine, debrisoquine, bretylium and reserpine. These group of drugs are also not routinely used at present for hypertension but reserpine in combination with hydralazine may be used in selected cases.*

Cost : Tab 250 mg (10) Rs. 15.00 - 34.00

Reserpine

I: Systemic hypertension.

C/I: Depression, severe renal failure, galactorrhoea, parkinsonism

P/C: Bronchial asthma, heart failure, active peptic ulcer, ulcerative colitis, digitalis intoxication, parkinsonism and phaeochromocytoma.

S/E: Sedation, depression, nasal congestion, excessive salivation, diarrhoea, orthostatic hypotension, weight gain, gynecomastia.

P/A: Tablets 0.25 mg.

Dose : 0.25 mg - 1 mg o.d.

Injection reserpine is not used for hypertensive crisis at present.

D/I: Digitalis, quinidines, MAO inhibitors and L-dopa cause drug interaction with reserpine.

Note: *Seldom used now due to high toxicity.*

Cost: Tab 0.25 mg (10) Rs. 0.63 - 1.00

5.7.7 Alpha adrenergic receptor blocking agents

Alpha blockers are currently gaining more acceptance as antihypertensive drugs. Their major problem have been first dose hypotension. These drugs are also useful in benign prostatic hyperplasia. The currently used alpha blockers in India are prazosin and terazosin.

Prazosin

I: Systemic Hypertension
Prostate hyperplasia.

C/I: Heart failure due to mechanical obstruction like aortic stenosis

P/C: May produce first dose hypotension and collapse. Withdraw diuretics if patient is already on diuretics. Reduce dose in renal

5 : Drugs used in Cardiovascular Disorders

impairment. Use with caution in pregnancy, the drug is preferably given at bed time.

S/E: Urinary frequency, incontinence, dizziness, headache, lack of energy, nausea, mild increase in the heart rate and mild increase in HDL cholesterol. It lowers total serum cholesterol. It may cause increase in renin levels.

P/A: Tablets 1 mg, 2 mg and 5 mg (sustained release)

Dose: Start with 0.5 mg h.s. If no syncope or giddiness in the morning, gradually increase dose to 1 mg b.d. In the extended release form of prazosin containing 5 mg the first dose effect is not common.

D/I: ACE inhibitors, alcohol, antidepressants, antipsychotics, anxiolytics, diuretics, betablockers and calcium channel blockers all potentiate the hypotensive action. Corticosteroids decrease the effect.

Cost: Tab 2 mg (10) Rs. 38.00 - 39.00

Terazosin

I: Systemic hypertension, benign prostatic hyperplasia.

C/I, P/C, S/E: Similar to prazosin

P/A: 1 mg, 2 mg, 5 mg tablets.

Dose: Give 1 mg at h.s. gradually increase dose upto 10 mg daily. Single daily dose is enough compared to prazosin.

D/I: Orthostatic hypotension potentiated by beta blockers, calcium channel blockers, diuretics. Synergistic effect with other antihypertensive drugs.

Cost: Tab 2 mg (10) Rs. 60.00 - 151.00

5.7.8 Drugs affecting the renin angiotensin system (ACE inhibitors)

These drugs can be divided into the angiotensin converting enzyme inhibitor and angiotensin II receptor antagonist. The converting enzyme inhibitor drugs have now become established as major antihypertensive drugs along with beta blockers, diuretics and calcium channel blockers. The mechanism of action is preventing the conversion of angiotensin I to angiotensin II. They also prevent degradation of bradykinin, which is a vasodilator.

The currently accepted indications for ACE Inhibitors are:

1. Systemic hypertension.
2. Diabetic nephropathy.
3. Congestive cardiac failure.
4. Myocardial infarction, in order to prevent adverse ventricular remodelling

Major problems with ACE Inhibitor drugs are:

1. Profound hypotension in some patients already on diuretics

2. Hyperkalemia.
3. Impairment of renal function.
4. May potentiate hypoglycemic effect of insulin and oral hypoglycemic drugs. They are contraindicated in pregnancy and in suspected cases of bilateral renal artery stenosis.

Captopril

Antihypertensive, anticardiac failure, vasodilator drug.

- I: Systemic hypertension, congestive cardiac failure, myocardial infarction (large, anterior MI to prevent adverse remodelling.)
- C/I: Known hypersensitivity to ACE inhibitors, suspected neurovascular disease, pregnancy, aortic stenosis and other LV outflow obstruction, porphyria.
- P/C: Reduce first dose if patient is on concomitant diuretic therapy. Watch for hyperkalemia if potassium sparing drugs are also given in renal impairment. Renal function is to be monitored before and during treatment.
- S/E: Persistent dry cough (most common side effect occurring in 10-20% of cases), taste alteration, blood dyscrasias (including agranulocytosis, neutropenia, aplastic anemia), thrombocytopenia, hyperkalemia, angioedema, proteinuria.
- P/A: Tablets 12.5 mg, 25 mg, 50 mg.
- Dose: In hypertension. 12.5 mg b.d. initially. It may be wise to start with even lower doses of 6.25 mg b.d. to avoid first dose hypotension and gradually increases the dose to 25 mg t.d.s. to get the desired clinical effect. Maximum daily dose is 75 - 100 mg.
- In CHF start with 6.25 mg b.d. Gradually increase to 25 mg t.d.s. under supervision.
- D/I: Alcohol, NSAIDS, anaesthetics, antidepressants, levodopa and chlorpromazine potentiate the hypotension caused by ACE inhibitors. Plasma concentration of digoxin is increased, lithium excretion is decreased. Corticosteroids, oestrogen and progesterone, preparations decrease the hypotensive effect.
- Cost: Tab 25 mg (10) Rs. 10.00 - 49.00

Enalapril ☆

I,C/I,P/C,S/E,D/I: Similar to captopril

P/A: Tablets 2.5 mg, 5 mg, 10 mg, 20 mg.

Dose: Systemic hypertension - 5 mg daily initially to be increased to 10 - 20 mg daily. Maximum dose is 40 mg. In cardiac failure dose is to be individualised.

Post MI start with 2.5 mg daily, and gradually increase to the usual maintenance dose of 5 - 10 mg in divided dose.

Cost: Tab 2.5 mg (10) Rs. 7.00 - 12.00

5 : Drugs used in Cardiovascular Disorders

Lisinopril

I, C/I, P/C: S/E, D/I: Similar to captopril

P/A: Tablets 2.5 mg, 5 mg, 10 mg.

Dose : Systemic hypertension to be increased to the 2.5 mg daily maintenance dose 10 - 20 mg upto a maximum dose of 40 mg single dose daily can be given.

CHF: 2.5 mg daily initial dose mg.

Maintenance dose 5 - 10 daily..

Post MI - 2.5 - 5 mg daily depending on the haemodynamic status of the patient. The drug may be discontinued after 6 weeks of the myocardial infarction if there is no heart failure.

Cost : Tab 2.5 mg (10) Rs. 15.00 - 20.00

Ramipril

I, C/I, P/C: S/E, D/I: Similar to captopril

P/A: Capsules 1.5 mg, 2.5 mg, 5 mg.

Dose : Hypertension: 1.25 mg daily increases to 2.5 - 5 mg daily.

CHF: 1.25 mg initially gradually increase if required.

Cost : Tab 2.5 mg (10) Rs. 40.00 - 41.00

Perindopril

I, C/I, S/E, P/C, D/I: Similar to captopril

P/A: Tablets 2 mg, 4 mg.

Dose : Start with daily dosage 2 mg daily increase to 4 mg daily depending on response.

Cost: Tab 4 mg (10) Rs. 246.00 - 247.00

5.7.9 Angiotensin II receptor antagonists

Properties are similar to ACE inhibitors but the major difference is that they do not affect the breakdown of bradykinins. The persistent cough of ACE I is thought to be bradykinin mediated. Hence these drugs may be useful in patients who have severe cough due to ACE inhibitor drugs.

Losartan

Antihypertensive.

I: Systemic hypertension

C/I: In pregnancy

P/C: May produce hyperkalemia. Use with caution in renal artery stenosis.

S/E: Giddiness, angioedema, hyperkalemia, rash.

P/A: Tablets 25 mg, 50 mg.

Dose : 50 mg o. d.

Start with a lower dose of 25 mg daily in patients using diuretics or in elderly patients.

D/I: Diuretics and other antihypertensives potentiate the action of losartan, risk of hyperkalaemia with potassium sparing diuretics. NSAIDs may blunt hypotensive effect of losartan .

Cost: Tab 25 mg (10) Rs. 40.00

CHAPTER 6 : DRUGS USED IN RESPIRATORY DISEASES

6.1 UPPER RESPIRATORY TRACT INFECTIONS

6.1.1 Common cold (Rhinitis)

Viral aetiology. Usually self limiting. Symptomatic treatment alone is required. Topical or systemic nasal decongestants and antihistaminics are used.

6.1.1.1 Topical Nasal Decongestants

These act by providing vasoconstriction locally by antihistaminic action.

Xylometazoline

I: Nasal congestion.

C/I: Glaucoma, pregnancy.

P/C: Prolonged use produces atrophic rhinitis and anosmia.

S/E: Dryness of mouth and throat, rebound congestion, allergic reaction.

P/A: Nasal drops 0.05%, 0.1 %

Dose: 0.05 – 0.1 % given as nasal drop.

D/I: Hypertension with MAO inhibitors and betablockers.

Cost: 0.1 % w/v(10 mL) Rs. 12.00 - 21.00

Oxymetazoline

I: Nasal conjunction.

C/I: Glaucoma, rhinitis sicca, acute porphyria.

P/C: Prolonged therapy exceeding 4 weeks. Young children, hypertension, coronary disease, hyper thyroidism, diabetes, pregnancy and lactation.

S/E: None reported.

P/A: Solution 0.01 %, 0.025 %, 0.05 %

Dose: 0.05 % given as nasal drops.

D/I: Avoid MAO inhibitors. Hypertensive crisis with antidepressants.

Cost: 0.05 % (10 mL) Rs. 20.00

Naphazoline

I:,C/I:, P/C:,S/E: Same as xylometazoline

6.1.1.2 Antihistamine

Azelastine hydrochloride

I: Allergic rhinitis.

C/I: Hypersensitivity, lactation.

P/C: Pregnancy, not to use longer than 6 months once after opening the bottle. Should not share the spray with others. Tip of the bottle should be dipped in boiled water, dried and capped appropriately after every use.

S/E: Nasal mucosal irritation, nasal bleeding.

P/A: Nasal spray 10 mL

Dose: Adults and children over 5 years 0.14 mL/metered dose. One spray into each nostril b.d.

Cost: Nasal spray (10 mL) Rs. 120.00

6.1.1.3 Sodium chloride

I: Nasal congestion.

P/A: Solution (0.9 %): 500 mL, 1000 mL

Dose: Sodium chloride (0.9%) given as nasal drop.

Cost: Solution (500 mL) Rs. 10.00

6.1.1.4 Sympathomimetics

Phenylephrine ☆

It is largely an indirect acting sympathomimetic drug similar in action to ephedrine but less stimulant to CNS.

I: Nasal congestion, sinusitis, common cold

C/I: Avoid excessive and prolonged use. Caution in infants under 3 months, patients with cardiac diseases, hypertension, hyperthyroidism and glaucoma.

P/C: Hyperthyroidism, cardiac diseases

S/E: Sneezing, mild burning sensation. After excessive use, tolerance with diminished effect - rebound congestion.

P/A: Capsules, Tablets, Syrup, Nasal drops. Most of the preparations contain other drugs like naphzoline, pheniramine maleate etc.

Dose: Orally 25 mg b.d. or q.d.s.

D/I: Prolongs the effect of local anaesthetics, hypotension with MAO inhibitors, antidepressants, ganglion blockers, reserpine and methyl dopa.

Cost: No pure preparation available. Only combination preparations.

Ephedrine

It is a systemically acting sympathomimetic drug. It also act locally to relieve nasal congestion.

I: Nasal congestion.

C/I: Debilitated patients, patient with impaired cough reflex, infants

6. Drugs used in Respiratory Diseases

P/C : Cardiac diseases

S/E : Restlessness, insomnia, tremors.

P/A : Drops 0.5 %.

Tablets 15 – 30 mg.

Dose : Oral decongestant Tablet 15 - 30 mg b.d. or t.d.s.

Syrup 5 mg b.d. or t.d.s.

0.5 % nasal drop, 1- 2 drops in each nostril b.d. or t.d.s.

D/I : Severe hypertension with MAO inhibitors. Alcohol and phenobarbitone antagonize the CNS stimulant action of ephedrine.

Cost : Drops (10 mL) Rs. 10.00

6.1.2 Allergic rhinitis and nasobroncheal allergy

Drugs are usually used as nasal sprays and nasal drops.

6.1.2.1 Mast cell stabilizers

Sodium Cromoglycate

This is an antiallergic agent acting by blocking the release of histamine by mast cells.

I : Prophylaxis of allergic rhinitis and asthma.

C/I : Hypersensitivity.

P/C : Pregnancy, lactation and neonates.

Presence of pus may prevent proper penetration of drug.

S/E : Bronchospasm, anaphylaxis, headache, sneezing and epistaxis.

P/A : Inhaler 1 mg/md, 5 mg/md, 20 mg/cartridge.

Spray 2 % w/v.

Dose : 2 squeezes q.d.s. Maintain with 1 squeeze t.d.s. (2 %)

D/I : None reported.

Cost : Inhaler 1mg/md (400 md) Rs. 161.00

6.1.2.2 Corticosteroids

Beclomethasone ☆

I : Allergic rhinitis and inflammatory conditions of the nose, bronchial asthma.

C/I : Hypersensitivity, systemic fungal infections, TB and diabetes.

P/C : Pregnancy, children < 5 years. Unhealed nasal infection previous treatment with oral steroids.

S/E : Local irritation, haemorrhagic secretion mild systemic steroid effects are produced. Candidial infection of mouth and throat Increased incidence of intranasal and paranasal infection.

P/A: Nasal spray 50 mcg, 100 mcg.

Dose: 2 sprays (100 mcg) into each nostril b.d.

D/I: None reported.

Cost: Inhaler 100 mcg (200 md) Rs. 150.00 - 220.00

Budesonide

I: Allergic rhinitis and inflammatory conditions of the nose, bronchial asthma.

C/I: Hypersensitivity.

P/C: Care in patients with pulmonary tuberculosis, fungal and viral infections in airway, pregnancy and lactation, patients should be instructed to rinse the mouth with water after each dosing.

S/E, D/I: None reported.

P/A: Inhaler 100 mcg/md.

Dose: Adults 100 - 200 mcg b.d. maximum 1600 mcg/day.

Children 50 - 100 mcg b.d. maximum 800 mcg/day.

Budesonide is not indicated for acute attacks of asthma.

Cost: Inhaler 100 mcg (400 md) Rs. 320.00

6.1.2.3 Oral Antihistamines

Astemizole

I: Allergic rhinitis

C/I: Pregnancy, hypersensitivity

P/C: To be given on an empty stomach. Use with caution in pregnancy and lactation.

S/E: Dry mouth, weight gain, diarrhoea and eczema.

P/A: Tablets 10 mg

Syrup 5 mg/5 mL

Suspension 1mg/mL

Dose: 10 mg daily. Maximum 30 mg / day.

D/I: Potentiates alcohol, MAO inhibitors, CNS depressants.

Cost: Tablets 10 mg (10) Rs.15.00-20.00

Syrup 5 mg/5 mL (60 mL) Rs.11.00- 16.00

Terfenadine

I: Allergic rhinitis, common cold.

C/I: Hypersensitivity

P/C: Liver disease, ECG abnormalities particularly QT prolongation

S/E: Drowsiness, fatigue, GI disturbances, dry mouth, epistaxis, photosensitivity, rash.

6. Drugs used in Respiratory Diseases

P/A: Tablet 50 mg, 60 mg, 120 mg.
Syrup 30 mg/5 mL.
Suspension 30 mg/5 mL.

Dose: 60 mg b.d.

Children 3 - 5 years: 15 mg b.d.

6 - 12 years: 30 - 60 mg b.d.

D/I: Cardiac arrhythmias with erythromycin, itraconazole and ketoconazole. Sedative effect with CNS depressants.

Cost: Tab	60 mg	(10)	Rs. 20.00 - 25.00
Syrup	30 mg/5 mL	(50 mL)	Rs. 14.00 - 24.00

Cetirizine HCl

I: Allergic rhinitis, seasonal rhinitis, chronic urticaria, allergic conjunctivitis and atopic dermatitis.

C/I: Pregnancy, lactation and hypersensitivity.

P/C: Pregnancy, renal impairment, elderly, driving, operating heavy machinery.

S/E: Drowsiness, GI disturbances, dry mouth and headache.

P/A: Tablet 10 mg
Syrup 1 mg/5 mL, 5 mg/5 mL.

Dose: 10 - 20 mg daily.

D/I: CNS depression with alcohol.

Cost: Tab	10 mg	(10)	Rs. 10.00 - 28.00
Syrup	5 mg/5 mL	(30 mL)	Rs. 13.00.

Loratidine

I: Allergic rhinitis and cold.

C/I: Hypersensitivity

P/C: Severe hepatic damage, pregnancy.

S/E: Nausea, fatigue

P/A: Tablet 10 mg

Dose: 10 mg o.d.

D/I: Ketoconazole and erythromycin will increase the plasma levels of loratidine.

Cost: Tab	10 mg	(10)	Rs. 22.00 - 40.00
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Fexofenadine

I: Allergic rhinitis, urticaria.

Dose: 120 mg/day

Ketotifen

- I: Allergic rhinitis, prophylaxis of asthma.
- C/I: Age < 2 yrs, acute asthma, hypersensitivity and pregnancy.
- P/C: Not to operate machinery after taking the drug.
- S/E: Drowsiness, dry mouth, weight gain, nausea and headache.
- P/A: Tablet 1 mg
Syrup 0.2 mg/mL, 1 mg/5 mL
- Dose: 1-2 mg b.d.
Children < 2 years : not recommended.
> 2 years ; 1 mg b.d.
- D/I: With oral hypoglycemic drugs it causes a fall in thrombocyte count.
Potentiates the action of sedatives and hypnotics.
- Cost: Tab 1 mg (10) Rs. 10.00 - 14.00
Syrup 1 mg/5 mL (100 mL) Rs. 41.00.

ANTIBIOTICS IN CURRENT USE IN RESPIRATORY INFECTIONS

(see individual sections)

- Penicillins : Penicillin G and Penicillin V
Penicillinase resistant penicillins - methicillin, cloxacillin
Broad spectrum penicillins - ampicillin, amoxycillin
Other penicillins : carbenicillin, ticarcillin, azlocillin, piperacillin
- Cephalosporines : 1st gen : cephalexin,
2nd gen : cefoxitin, cefuroxime
3rd gen : ceftazidime, cefotaxime
4th gen : cefpirome, cefepime
- Aminoglycosides : gentamicin, tobramycin, amikacin, netilmycin, streptomycin, kanamycin.
- Macrolides : erythromycin, roxithromycin, azithromycin, clarithromycin.
- Co-trimoxazole : trimethoprim - sulfamethoxazole
- Tetracyclines: tetracycline, doxycyclin
- Quinolones : ciprofloxacin, ofloxacin, pefloxacin, sparfloxacin
- Newer beta lactams : aztreonam, imipenem
- Vancomycin : vancomycin
- Lincosamide : clindamycin, lincomycin
- Synergistic combination : amoxycillin + cloxacillin
ampicillin + cloxacillin
amoxycillin + clavulanic acid
ticarcillin + clavulanic acid

6.2 DRUGS USED IN TUBERCULOSIS

These include isoniazid, rifampicin, pyrazinamide, ethambutol, streptomycin and others.

Isoniazid (INH, Isonicotinic acid hydrazide) ☆

I: Treatment of tuberculosis, bactericidal against actively multiplying *M. tuberculosis*, *M. bovis* and *M. kansasii*. This is the most powerful and most extensively used antituberculosis drug.

C/I: Hypersensitivity, hepatic insufficiency and psychosis.

P/C: Monitor serum level of hepatic transaminases.

Patients at risk of peripheral neuropathy (malnutrition, chronic alcoholism, diabetes and others) should additionally receive pyridoxine 20 mg dose.

Epilepsy should be controlled effectively since INH may provoke attack.

S/E: Hepatotoxicity - The incidence of INH induced hepatitis increase with age, alcohol consumption and alcoholic liver disease. INH induced hepatitis usually resolves after discontinuation of the drug. Transient elevation of serum transaminase may occur, but resolves as drug therapy continues. This is not a contraindication for INH. Peripheral neuropathy is dose-related, probably due to increased excretion of pyridoxine. Patients with malnutrition and those predisposed to neuropathy by diabetes, alcoholism or uremia, pregnant women and those with seizure disorders should be supplemented with pyridoxine - 20 mg daily.

P/A: Oral - tablet and liquid

Parenteral preparation can be given i.v. or i.m. in special circumstances at the same as oral dose on those who cannot ingest orally.

Dose: 5 mg/kg bw Single dose.

Adult : 300mg o.d.

600 mg (10mg/kg) for intermittent regimen and for nervous system disease.

450 mg daily - in tuberculous meningitis.

D/I: The effects of anticonvulsants may be increased. Antacids may reduce the absorption of INH.

Cost : Tab 300 mg (10) Rs. 9.00

Rifampicin ☆

It acts by inhibiting the synthesis of nucleic acids.

I: Bactericidal and sterilizing drug for the treatment of tuberculosis. Bactericidal for most species of *Mycobacterium*. It is also used for the treatment of leprosy.

- C/I: Hypersensitivity, severe liver disease. Thrombocytopenia and acute renal failure are absolute contraindications.
- P/C: Patient should be warned about the orange discolouration of body secretions and urine. It can permanently discolor soft contact lenses otherwise it is harmless.
- S/E: Flu like syndrome in intermittent dosage. Nausea, vomiting, muscle cramps, jaundice, and CNS disturbances, Skin reactions, eosinophilia, transient leukopenia, thrombocytopenia, shock, drowsiness, headache, ataxia, visual disturbances and menstrual irregularities.
- P/A: Capsules 150, 300, 450, 600 mg
Tablet 450, 600 mg
Syrup 100 mg/5 mL
- Dose: 10 mg/kg - oral single dose. 450mg for adults, 600mg for patients more than 60 kg weight.
The drug should be given on an empty stomach and fluids and food should be taken only after 1 h.
- D/I: It reduces the effectiveness of oral contraceptives, corticosteroids, phenytoin, oral antidiabetics, oral anticoagulants and disopyramide by inducing hepatic metabolism. It reduce Vitamin D blood levels. Severe hepatitis when used along with isoniazid. Food will delay the absorption. Fixed drug combination are used to increase compliance.
- | | | | | |
|--------|-------|-------------|----------|-------------------|
| Cost : | Caps | 450 mg | (10) | Rs. 65.00 - 70.00 |
| | Tab | 450 mg | (10) | Rs. 68.00 - 72.00 |
| | Syrup | 100 mg/5 mL | (200 mL) | Rs. 63.00 - 68.00 |

Pyrazinamide (PZA) ☆

Bactericidal to M.tuberculosis - sterilizing especially to intracellular organism

I: Treatment of tuberculosis.

The only one drug acting in the acidic pH. Intracellular organisms are killed. Bactericidal and sterilizing action - effective in the initial intensive phase. M.bovis is resistant to PZA.

C/I: Hypersensitivity, pregnancy, existing liver disease and gout.

P/C: Patients with diabetes should be carefully monitored since blood sugar levels may become labile. Gout may be exacerbated.

S/E: Arthralgia, loss of appetite, malaise, nausea, and liver damage.

P/A: Tablet 500 mg, 750 mg, 1000 mg and 1500 mg.

Dose: 20- 35 mg/kg oral. One or two divided doses.

D/I: Alters the action of oral antihypoglycemic agents and disturbs blood glucose levels. It decreases the serum INH concentration.

Cost :	Tab	750 mg	(10)	Rs. 25.00 - 30.00
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6. Drugs used in Respiratory Diseases

Ethambutol ☆

It acts by possibly inhibiting RNA synthesis and also by affecting metabolism of cell wall.

- I: Treatment of tuberculosis. Bacteriostatic drug in usual dosage. (Bactericidal in higher dosage). It is used in combination with other drugs to prevent or delay the emergence of resistant strains.
- C/I: Optic neuritis, hypersensitivity, reduction of visual acuity - particularly inability to distinguish red and green. (eg. young age)
- P/C: Patients should be advised to discontinue treatment immediately and to report to the doctor if visual disturbances occur.
- S/E: Retrobulbar neuritis with reduction of visual acuity. Reduced renal clearance of urates. G.I disturbances, anorexia, false positive test for phaeochromocytoma.
- P/A: Tablet 200 mg, 400 mg, 800 mg, 1000 mg
- Dose: 15-25 mg/kg bw. Single dose - oral.
- D/I: Absorption delayed or reduced by aluminum hydroxide. Synergistic effect with other antituberculous agents.
- Cost: Tab 800 mg (10) Rs. 18.00 - 22.00

Streptomycin ☆

- I: Aminoglycoside antibiotic. It acts by inhibiting protein synthesis. It was used as one of the powerful antituberculosis drug along with INH prior to the introduction of short course chemotherapy with rifampicin and other drugs. It is a bactericidal drug which has to be given by i.m. injection over several months for its effect. Another disadvantage is the readiness of M.tuberculosis to develop resistant against streptomycin. Due to this reason at present it is used only as a reserve drug under special circumstances. Use is restricted to tuberculosis treatment as a component of several combined antituberculosis chemotherapeutic regimens.
- C/I: Hypersensitivity, renal or hepatic insufficiency, premature infants, pregnancy and myasthenia gravis.
- P/C: Avoid concurrent use of other ototoxic and nephrotoxic drugs.
- S/E: Anaphylactic shock. Vestibular dysfunction leading to giddiness and vertigo which may be persistent for several months even after stopping the drug. Nerve damage may occur in some cases but it was more common with dihydrostreptomycin which is not commonly used at present.
- P/A: Injection 0.75 g, 1 g vial.
- Dose: 0.75 g - 1 g i.m.daily for adult, 15-20 mg/kg in children for 2 months in the initial intensive phase.
- D/I: Potentiate nephrotoxicity and ototoxicity produced by other aminoglycosides and cephalosporin, cisplatin, vancomycin. Ototoxicity potentiated by frusemide. Plasma level will be increased

by indomethacin. Synergism with benzyl penicillin – when this combination is used for treating other infections. Potentiates the effect of neuromuscular blocking agents administered during anaesthesia.

Cost: Inj 0.75 g (vial) Rs. 5.00 - 6.00

The Government provides the drugs for the total treatment period free of cost to the patients who come under the National TB control programme both hospital and domiciliary treatment. Single drug should not be used for the treatment of tuberculosis. Combination packs are available for RNTCP programme.

INH, rifampicin, pyrazinamide and ethambutol in combination for two months as initial intensive chemotherapy followed by INH and rifampicin for four months of continuation phase. If resistance is suspected streptomycin is added to the intensive phase and ethambutol in the continuation phase and the duration will be extended for total nine months.

Note: The National Tuberculosis Control Programme of the Government of India has given clear guidelines for the treatment of tuberculosis. It is essential that these guidelines are adhered to when mass treatment in our hospitals is required. When undertaking the treatment of individual cases the regimen can be modified depending upon the effectiveness of the drug combination, cost, convenience affordability co-morbidity and patient acceptability. In no case should incorrect drug combination or incomplete therapy be administered since these are the most common reasons to develop drug resistance in M.tuberculosis infection.

6.2.1 RNTCP treatment regimen

TB treatment	TB Patients	Intensive Phase	Continuation Phase
Category I	New smear - positive		
	New smear - negative (seriously ill)	2(HRZE) ₃	4(HR) ₃
Category II	Extra-pulmonary **	2(SHRZE) ₃	5(HRE) ₃
	- Relapse ***	1(HRZE) ₃	
	- Failure ***		
	- Treatment After Default		
Category III	New smear-negative (not seriously ill)	2(HRZ) ₃	4(HR) ₃
	Extra-pulmonary (not seriously ill)		

* The number before the letters refers to the number of months of treatment. The subscripts after the letters refers to the number of

6. Drugs used in Respiratory Diseases

doses per week. H : Isoniazid (600 mg), R : Rifampicin (450 mg), Z : Pyrazinamide (1500 mg), E : Ethambutol (1200 mg), S: Streptomycin (750 mg). Patients who weigh more than 60 kg receive additional rifampicin 150 mg. Patients more than 50 years old receive streptomycin 500 mg. Patients in categories I and II who have a positive sputum smear at the end of the initial intensive phase receive an additional month of intensive phase treatment.

** Examples of seriously ill extra-pulmonary TB cases are meningitis, disseminated TB, tuberculous pericarditis, peritonitis, bilateral or extensive pleurisy, spinal TB with neurological complications and intestinal and genito-urinary TB.

*** Very rarely, patients relapse with extra-pulmonary or smear-negative pulmonary tuberculosis; such patients are considered as 'Other' and treated with the Category II regimen.

6.2.2 Reserve drugs

Kanamycin

Aminoglycoside antimicrobial

I: Used as a second line drug to treat resistant tuberculosis.

C/I: Pregnancy, renal failure and hypersensitivity.

P/C: Breast-feeding. Monitor blood levels when the renal function is impaired.

S/E: Fever, rash, exfoliative dermatitis, itching, nausea, and headache, neurotoxicity, nephrotoxicity, thrombocytopenia.

P/A: Injection 0.5 g, 1 g vial.

Dose: 15 mg/kg, 0.5 – 1 g i.v./i.m. twice or thrice weekly.

D/I: It potentiates the neuromuscular block by action of muscle relaxants used in anaesthesia. May be inactivated by beta-lactam antibiotics. Frusemide increases the nephrotoxicity.

Cost : Inj 1 g (vial) Rs. 22.00 - 26.00

Capreomycin

This is an aminoglycoside drug.

I: As a second line drug in combination while treating drug resistant tuberculosis.

C/I: Hypersensitivity, pregnancy and renal disease.

P/C: Use with caution in lactation, monitor renal function periodically.

S/E: Fever, abnormalities in liver function, vertigo, leukopenia and hypokalemia, toxic nephritis.

P/A: Injection 0.5 g, 0.75 g, 1 g, vial.

Dose: 500 mg - 1 g i.m. daily. 15-20 mg / kg / day.

D/I: Co-administration of aminoglycosides increases the risk of respiratory paralysis and renal dysfunction.

Cost : Inj 0.5 g , (vial) Rs. 105.00 - 115.00

Cycloserine

I: This is a second line antitubercular drug used in the treatment of resistant cases. It acts by inhibiting the cell walls synthesis.

C/I: Psychosis, epilepsy, severe anxiety, alcohol dependence, depression, and renal failure.

P/C: Discontinue if allergy or CNS toxicity occurs. Reduce dose in renal impairment.

S/E: Causes Vit. B₁₂ and folic acid deficiency. Nervousness, headache, convulsions, suicidal attempts, and psychotic states.

P/A: Tablet 250 mg

Dose: 10 mg/kg /day - orally 250-500 mg b.d.

D/I: Alcohol increases the risk of convulsions. INH and ethionamide increases CNS toxicity. Plasma level of phenytoin increases to toxic levels.

Cost : Tab 250 mg (10) Rs. 290.00 - 300.00

Ethionamide

Bacteriostatic against Mycobacterium tuberculosis and other atypical mycobacterium.

I: As a second line drug to treat resistant tuberculosis.

C/I: Hepatic dysfunction

P/C: Psychiatric illness, pregnancy, and lactation.

S/E: G.I upsets, acne, alopecia, convulsions, diplopia, psychological disturbances, thrombocytopenia, gynaecomastia, impotence.

P/A: Tablet 125 mg, 250 mg

Dose: 12-15 mg/kg/day. 0.5 - 1.0 g in two divided doses daily.

D/I: Convulsions may occur when used with cycloserine. Glycemic control may be difficult in diabetic patients.

Cost : Tab 250 mg (10) Rs. 120.00 - 130.00

Prothionamide

An ethionamide derivative active against M.tuberculosis. Action is similar to that of ethionamide. Resistance develops generally if it is used alone. Prothionamide is better tolerated than ethionamide.

I: As a second line drug for the treatment of drug resistant tuberculosis.

C/I: Gout, hypersensitivity, and hepatic dysfunction.

P/C: Pregnancy, lactation, and children. Liver function monitoring is

6. Drugs used in Respiratory Diseases

required. Rifampicin and prothionamide combination use should preferably be avoided.

S/E: Elevation of plasma uric acid leading to gouty arthritis. GI symptoms, depression, sleepiness.

P/A: Tablet 250 mg

Dose: 250mg orally t.d.s. for adults. 15 - 20 mg for children.

D/I: Alters the action of oral hypoglycemic agents, alters the serum INH concentration.

Cost : Tab 250 mg (10) Rs. 145.00 - 155.00

Para Aminosalicyclic Acid (PAS)

This is a bacteriostatic drug for M.tuberculosis used prior to the development of the present day short course chemotherapy. PAS was a first line drug in the treatment of tuberculosis. Though its antituberculosis action is weak, it acts well to prevent the development of drug resistance against INH and streptomycin. At present PAS is only seldom used. It reduces the chance of developing resistance to INH.

I: Resistant tuberculosis as a companion drug.

C/I: Hepatic and renal disorders

S/E: GI upset. Hepatic and renal toxicity, thrombocytopenia and hypokalemia. Prolonged use may produce goiter and hypothyroidism. Urine show reducing agent - interferes with Benedict's reagent and this may be mistaken for glycosuria occurring in diabetes mellitus.

P/A: Tablet 0.5 g

Granules 100 mg

Dose: 300 mg/kg/day oral. 12-15g in two divided dose for adults.

D/I: It reduces the absorption of rifampicin if taken together.

Cost : Granules 100 mg (10) Rs. 190.00 - 200.00

Quinolones : Ciprofloxacin and sparfloxacin, ofloxacin. (see section 2.2.8)

Macrolides: Roxithromycin and clarithromycin (see section 2.2.5)

Some points to be noted are:

1. Refer cases which are difficult to diagnose, to a chest specialist.
2. Do not attempt modifications of regimen.
3. Consult chest physician in case of adverse effect to drugs
4. Never attempt to treat resistant or suspected resistant cases. Refer to a chest specialist.

Management of multi drug resistant tuberculosis is a very serious and disturbing problems, demanding the use of several second line drugs which are only weakly effective but are

moderately toxic several other drugs such as quinolones, including ciprofloxacin and sparfloxacin, macrolides such as roxithromycin and clarithromycin are used in salvage chemotherapy. If clearance of the drug resistant organism is not achievable by chemotherapy surgical excision to remove the focus of infection should be considered. Because of the above reason the management of such cases should preferably be done by a specialist.

6.3 DRUGS USED IN THE TREATMENT OF AIRWAY DISEASES

6.3.1 Asthma and Chronic Obstructive Pulmonary Disease (COPD)

6.3.1.1 Bronchodilators (Beta -2 adrenergic agonists)

Salbutamol ☆

I: Asthma acute and chronic forms, COPD, prophylaxis of exercise induced asthma

C/I: Thyrotoxicosis, hypersensitivity, premature labour.

P/C: Patients with arrhythmias, elderly, pregnant women, those on other sympathomimetic drugs.

S./E: Muscle tremor, tachycardia, hypokalemia, restlessness, muscle cramps.

P/A: Tablets 2mg, 4 mg

Capsules 4 mg, 8mg

Inhaler 100mcg/md

Syrup 2mg/5mL

Dose: Oral tablets : 2-4 mg t.d.s. Children 2 mg t.d.s. Sustained release preparation : 4-8 mg b.d.

Inhaler : 100 - 200 mcg t.d.s or q.d.s.

Rotahaler : 200 - 400 mcg t.d.s. or q.d.s..

Nebuliser : 5 mg / mL. Dose : 2.5 - 5 mg diluted with saline t.d.s or q.d.s.

D/I: Hypokalemia with steroids and diuretics, potentiates the vascular effects of MAO inhibitors and tricyclic antidepressants. Effects are antagonized by beta blockers.

Cost : Tab 2mg (10) Rs.2.00-5.00

Cap 4 mg (10) Rs.8.00

Inhaler 100mcg/md (200md) Rs.67.00

Terbutaline

I: Asthma acute and chronic forms, COPD, prophylaxis of exercise induced asthma.

C/I: Thyrotoxicosis, hypersensitivity, premature labour.

6. Drugs used in Respiratory Diseases

P/C : Patients with arrhythmias, elderly, pregnant women, those on other sympathomimetic drugs.

S./E: Muscle tremor, tachycardia, hypokalemia, restlessness, muscle cramps.

P/A: Tablets 2.5mg, 5 mg and 7.5 mg

Inhaler 250 mcg/md

Syrup 1.5 mg/5mL

Injection 0.5 mg/mL

Dose : Oral tablets : Adults 2.5 - 5 mg b.d. or t.d.s.

Children 1.5 - 3 mg b.d. or t.d.s.

Durules : 5 - 7.5 mg b.d.

Inhaler : 250 - 500 mcg t.d.s or q.d.s.

Nebuliser : 10 mg/mL. Dose 5 - 10 mg diluted with saline upto 4 times per day.

Injections : given subcutaneously 0.25 mg upto 4 times per day.

D/I: Hypokalemia with steroids and diuretics, potentiates the vascular effects of MAO inhibitors and tricyclic antidepressants. Effects are antagonised by beta blockers.

Cost :	Tablets 5 mg	(10)	Rs.15.00-18.00
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Inhaler	250mcg/md	(200md)	Rs.76.00
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Syrup	1.5mg/5mL	(100mL)	Rs.16.00
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Injection	0.5mg/mL	(5x1mL)	Rs.30.00
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Salmeterol

Long acting beta 2 agonist.

I: Long term prevention of symptoms especially nocturnal symptoms. Prevention of exercise induced bronchospasm.

C/I: Hypersensitivity, acute asthma, thyrotoxicosis.

P/C: Not useful for acute attacks, patients with seizures, coronary artery disease, pregnancy and lactation.

S./E: Tremors, palpitation, tachycardia, headache and muscle cramps.

P/A: Inhaler 25 mcg/md (120 md, 200 md)

Rotacap 50 mcg

Dose : Inhaler : 2 puffs (50 mcg) b.d.

Rotahaler : 1 rotacap b.d.

D/I: Hypokalemia with steroids and diuretics, potentiates the vascular effects of MAO inhibitors and tricyclic antidepressants. Effects are antagonised by beta blockers.

Cost :	Inhaler 25 mcg/md	(120md)	Rs. 93.00-98.00
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Rotacap	50mcg	(30)	Rs.40.00
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6.3.1.2 Anticholinergics

Ipratropium Bromide

- I: COPD, relief of acute bronchospasm especially in patients with intolerance to beta 2 agonists, drug of choice for bronchospasm due to beta blocker medication.
- C/I: Hypersensitivity
- P/C: Narrow angle glaucoma, pregnancy, lactation, prostatic hypertrophy.
- S/E: Dry mouth, paradoxical bronchoconstriction, glaucoma.
- P/A: Inhaler 20 mcg/puff 200md
- Dose: 1 - 2 puffs (20 - 40) mcg t.d.s. or q.d.s.
- D/I: None reported.
- Cost : Inhaler 20 mcg/puff (200md) Rs.131.00

Theophylline ☆

This drug acts by directly relaxing the smooth muscle of the bronchi.

- I: Acute asthma, long term control and prevention of symptoms, COPD.
- C/I: Hypersensitivity, neonates, lactation.
- P/C: Hypertension, myocardial infarction, hyperthyroidism, pregnancy, lactation, hepatic disease and acid peptic disease,
- S/E: Nausea, vomiting, gastric disturbances, headache, gastric reflux, diuresis, cardiac arrhythmias, epilepsy.
- P/A: Tablets 200mg,300mg,400mg,600mg
Capsule 100mg,200mg, 250mg
Injection 2mL ampoule
Syrup 20mg/mL
- Dose: Etophylline 169.4 mg/mL i.v. dose 2 mL 8hrly.
Oral dose : 80 - 240 mg t.i.d.
Children : 24 mg/kg/bw in divided doses.
Controlled release preparation : 400 - 600 mg o.d.
- D/I: Metabolism is enhanced by rifampicin, phenobarbitone and alcohol, while it is reduced by ciprofloxacin, cimetidine, erythromycin and allopurinol.
- Cost : Tab 200mg (10) Rs.9.00-15.00
Inj (2mL ampoule) Rs.3.00
Syrup 20mg/mL (100mL) Rs.11.00

Aminophylline ☆

- I: Asthma, COPD, congestive cardiac failure, respiratory failure.
- C/I: Acid peptic disease, seizures, hypersensitivity.

6. Drugs used in Respiratory Diseases

- P/C : Neonates, children, pregnancy, lactation, cardiac arrhythmias and hepatic diseases.
- S/E : Hypotension, neurotoxicity, seizures, nausea, vomiting, insomnia, headache, CNS stimulation.
- P/A : Tablets 100mg
Injection 250mg/2mL
- Dose : Initial loading dose : 4 - 6 mg/kg.
Maintenance dose : 3 - 4 mg/kg.
Children : 5 mg / kg
- D/I : Increases risk of arrhythmias with sympathomimetics and halothane. Tachycardia with pancuronium. Metabolism inhibited by beta blockers.
- Cost : Tab100mg (1000) Rs.96.00
Inj 250mg/2mL (10mL) Rs.7.00

6.3.1.3 Systemic steroids

These act by relieving the inflammation of the broncheal mucosa in asthma. They are very potent and antiasthmatic drugs which are active when given orally, and for rapid action parenterally or directly into the bronchial tree by aerosols. They relieve acute attacks immediately. They also prevent the onset of acute paroxysms. Corticosteroids may be given in a moderate dose or high dose short time basis for few days or in the minimum effective dose on a long term basis, for symptom relief. Long term corticosteroid produce several adverse side effects and therefore it should be the aim to withdraw these as early as possible. Still a few persons become steroid dependent.

Prednisolone ☆

- I : 1. Long term prevention of asthma symptoms.
2. Treatment of tachyphylaxis to beta agonists
3. Allergic diseases
4. Auto immune diseases
5. Malignancy
- C/I : Hypersensitivity, systemic infections, live virus immunization, peptic ulcer, tuberculosis.
- P/C : Pregnancy, diabetes mellitus, osteoporosis, glaucoma, hypertension, congestive heart failure.
- S/E : Fluid and electrolyte balance impairment, moon face, trunkal obesity, fragile skin, psychosis, delayed wound healing.
- P/A : Tablet 5 mg, 10 mg and 20 mg.
Injection 40 mg/mL (ampoule), 500 mg and 1000 mg (vial).

Dose : 80 - 120 mg / day. Gradually taper off the dose.

D/I: Action is reduced by antiepileptics, rifampicin, cyclosporine. Lowers plasma salicylate levels. Increases the requirement of insulin and oral hypoglycemic agents.

Cost :	Tab	10 mg	(10)	Rs. 12.00 - 15.00
	Inj	40 mg/mL	(2 mL)	Rs. 50.00 - 70.00
	Inj	500 mg	(vial)	Rs. 440.00 - 450.00

Hydrocortisone

I: Acute asthma, allergic reactions, anaphylaxis, Addison's disease

C/I: Hypersensitivity, systemic infections, live virus immunization, peptic ulcer, tuberculosis.

P/C: Pregnancy, diabetes mellitus, osteoporosis, glaucoma, hypertension, congestive heart failure.

S/E: Fluid and electrolyte balance impairment, moon face, trunkal obesity, fragile skin, psychosis, delayed wound healing, avascular necrosis of the head of femur.

P/A: Injection 25 mg, 100mg, 200mg, 400mg

Dose : 100 - 500 mg i.v. t.d.s. or q.d.s.

D/I: Action is reduced by antiepileptics, rifampicin, cyclosporine. Lowers plasma salicylate levels. Increases the requirement of insulin and oral hypoglycemic agents.

Cost : Inj 100mg (vial) Rs. 31.00 - 34.00

6.3.1.4 Inhaled Steroids

Corticosteroids can be delivered directly into the respiratory tract in the form of aerosols through nebulizers, metered dose inhalers and rotahalers. The dose is also considerably smaller compared to oral and parenteral drugs. Adverse side effects are much less. When the drug is delivered as a inhalation only part of it reaches the respiratory tract, the rest of it is swallowed.

Beclomethasone

I: Long term prevention of asthma.

C/I: Acute asthma, hypersensitivity.

P/C: Pregnancy, lactation, local fungal infections.

S/E: Hoarseness, candidiasis.

P/A: Inhaler 50mcg, 100mcg, 200mcg, 250mcg
Spray 50mcg/md
Rotacap 100mcg

Dose : 400 - 800 mcg/ day in 2 - 4 divided doses.

Children : 50 - 100 mcg / day.

D/I: None reported

6. Drugs used in Respiratory Diseases

Cost :	Inhaler 100mcg	(200md)	Rs. 150.00
	Rotacap 100mcg	(30)	Rs. 40.00

Budesonide

I:	Long term prevention of asthma		
C/I:	Acute asthma, hypersensitivity.		
P/C:	Pregnancy, lactation, local fungal infections.		
S/E:	hoarseness, candidiasis.		
P/A:	Inhaler 100mcg/md		
Dose:	100 - 200 mcg b.d. Max 1600 mcg / day		
	Children 50 - 100 mcg b.d.		
D/I:	None reported		
Cost :	Inhaler 100mcg/md	(100md)	Rs.146.00

Fluticasone propionate

Glucocorticoid twice as potent as budesonide and beclomethasone.

I:	Preventive therapy of asthma		
C/I:	Hypersensitivity, age < 4 yrs, acute asthma		
P/C:	Pregnancy, lactation, children.		
S/E:	Candidiasis, hoarseness		
P/A:	Inhaler 50mcg, 125 mcg		
	Rotacaps 100mcg, 250mcg		
	Cream 0.05 % w/w		
Dose:	Adults : 250 - 500 mcg/ day		
	Mild persistent asthma : 100 - 250 mcg		
	Moderate persistent : 250 - 500 mcg		
	Severe persistent : 500 - 1000 mcg		
	Children : 50 - 100 mcg/ day		
D/I:	None reported.		
Cost :	Cream 0.05% w/w (5 g)		Rs. 28.00 - 35.00
	Inhalers (125 mcg)		Rs. 350.00
	Rotacap (30)		Rs. 50.00

Compared to salbutamol inhaler, corticosteroids are less potent immediate bronchodilators. Their main role is to prevent asthmatic paroxysm therefore they may be given as regular night time dose of 100 - 200 mcg/day. Asthmatic attacks are managed by inhalation of salbutamol. Preparations containing both corticosteroids and salbutamol are available.

5.3.1.5 Mast Cell stabilizers

Sodium cromoglycate

- I: Long term prevention of asthma symptoms, preventive therapy prior to exposure to known allergen or exercise.

- C/I: Hypersensitivity.
P/C: Neonates, pregnancy and lactation
S/E: Cough, rash, urticaria, bronchospasm.
P/A: Inhaler 1 mg/md, 20 mg/cartridge
Dose: 2 puffs q.d.s. (1 mg / puff)
D/I: None reported
Cost: Inhaler * 1 mg/md (400md) Rs. 161.00

Nedocromil sodium

- I: Long term prevention of asthma symptoms, preventive therapy prior to exposure to known allergen or exercise.
C/I: Hypersensitivity.
P/C: Neonates, pregnancy and lactation
S/E: Cough, rash, urticaria, bronchospasm.
P/A: Inhaler 2 mg/md, 20 mg/cartridge
Dose: By aerosol inhalation, 4mg (2 puffs) b.d. increase to q.d.s. if necessary,
Children under 12 years, not yet recommended.
Cost: Not freely available.

Ketotifen

- I: Prophylaxis of asthma, food allergy.
C/I: Diabetics on oral hypoglycemic agents, neonates(children under 2 years), hypersensitivity, pregnancy, lactation, acute attacks of asthma.
P/C: Previous anti-asthmatic treatment should be continued for a minimum of 2 weeks after initiation of ketotifen treatment. Pregnancy and breast feeding.
S/E: Drowsiness, dry mouth, slight dizziness, CNS stimulation, weight gain also reported.
P/A: Syrup 1 mg/5 mL.
Tablet 1 mg.
Dose: 1 mg b.d. with food increased if necessary to 2 mg b.d.; Initial treatment in readily sedated patients 0.5 to 1 mg at night.
Children : Over 2 years, 1mg b.d.
D/I: Potentiate the effects of sedatives, hypnotics, antihistamines and alcohol. Reversible fall in platelet count with concomitant use of oral antidiabetics.
Cost: Syr 1 mg/5 mL (60 mL) Rs. 23.00 - 42.00
Tab 1 mg (10) Rs. 10.00 - 15.00

6. Drugs used in Respiratory Diseases

6.3.1.6 Leucotriene receptor antagonist

Zafirlukast

- I: Long term control and prevention of symptoms in mild persistent asthma for patients > 12 years of age
- C/I: Children
- P/C: Food reduces the absorption of the drug. So taken 1 h prior to or 2 h after food.
- S/E: None reported so far
- P/A: Tablet 20 mg
- Dose: 20 mg b.d.
Montelukast: o.d. headache
- D/I: Inhibits warfarin metabolism.
- Cost: Not freely available.

6.3.1.7 5-lipo oxygenase inhibitor

Ziluton

- I: Long term control and prevention of symptoms in mild persistent asthma for patients > 12 years of age
- C/I: Children
- P/C: Monitor liver enzymes
- S/E: Hepatitis, hyperbilirubinemia and elevated liver enzymes.
- P/A: Tablet
- Dose: 600 mg q.d.s.
- D/I: Inhibits the metabolism of terfenadine, warfarin and theophylline.
- Cost: 'Not freely available.

6.3.1.8 Antigens for immunotherapy.

- I: Nasobronchial allergy, food allergy, certain forms of skin allergy.
- C/I: Below 5 years or above 60 years.
- P/C: Treatment must be done under the advice of an allergologist.
- S/E: No serious side effects if the schedule supplied by the allergologist is followed.
- P/A: Injectable vials.
- Dose: As per schedule
- D/I: None reported.
- Cost: Inj (1 vial) Rs. 100.00-150.00

6.3.2 Newer drug delivery systems in asthma

Metered Dose Inhalers

Use chlorofluorocarbon propellant to carry the suspended drug particle at a great speed towards the pointed direction.

Drugs available are : Salbutamol, terbutaline, salmeterol, beclomethasone, budesonide, fluticasone, ipratropium and cromoglycate.

Precautions : Good hand mouth coordination is required and good inhaler technique is also a must. The success of inhalation therapy depends upon perfecting the technique of inhalation so as to deliver the maximum amount into the tracheobroncheal tree. This should be taught to the patient and the physician should satisfy himself that the technique is mastered. So also inhalation should be taken at the earliest warning of asthma since inhalation will be ineffective if the paroxysm sets in. One of the frequent causes of failure if inhaled medication is improper technique.

In patients with poor hand mouth coordination, a spacer device is advisable in which the drug is delivered into a spacer and the patient inhales from this.

Dry Powder Inhalers

Here the drug is loaded as a capsule containing micronized particles in a lactose carrier called the rotacap. The apparatus used is called a rotahaler.

Drugs available are : Salbutamol, salmeterol, beclomethasone, budesonide and fluticasone.

Nebulizers

Nebulized drugs are delivered by a gas flow driving a jet nebulizer unit, which produces the aerosol, or by an electric ultrasonic nebulizer.

Drugs that are used with nebulizer : Salbutamol, terbutaline, ipratropium, budesonide and acetyl cystine. The advantage of nebulizer is that the aerosol reaches the respiratory tract along with inhaled air or oxygen without extra effort by the patient. Therefore this is the method of choice when asthma is severe.

Aminophylline is reserved for those unresponsive to the maximal dose of beta 2 agonists. Dose is initially, 5 mg/kg., then 0.5 mg/kg/h as i.v. drip.

6.4 RESPIRATORY STIMULANTS

Classification

1. Analeptics : Nikethamide, doxapram
2. Methyl xanthines : Theophyllines
3. Hormones : Medroxyprogesterone
4. Tricyclic antidepressants : Protriptyline
5. Carbonic anhydrase inhibitor : Acetazolamide
6. Triazine derivative : Almitrine bimesylate

6. Drugs used in Respiratory Diseases

Doxapram

- I: Acute respiratory failure, post-operative respiratory failure, laryngospasm following intubation, drug induced CNS depression
- C/I: Heart disease, epilepsy, cerebral oedema, phaeochromocytoma, recent cerebro vascular accidents.
- P/C: Pulmonary embolism, pneumothorax, neonates, pregnancy and liver diseases.
- S/E: Hypertension, tachycardia, fasciculations and dyspnoea
- P/A: Injection 20mg 5mL, 20 mL
- Dose: 1.5 - 4 mg/min i.v. infusion. Repeat every 1 - 2 h till the patient wakes up.
- D/I: Produces agitation with theophyllines
- Cost: Inj 20mg (5mL) Rs.33.00

Theophylline (see section 6.3.1.2)

Protriptyline

- I: Respiratory failure, sleep apnoeas.
- C/I: Same as tricyclic antidepressants. Alcoholism, asthma, bipolar disorders, GI disorders, blood disorders, glaucoma, hyperthyroidism, schizophrenia, seizure disorders, urinary retention.
- P/C: Monitor cardiovascular parameters in elderly if dose exceeds 20 mg/day.
- S/E: Dry mouth, constipation
- P/A: Tablet 5 mg, 10 mg.
- Dose: 15 to 40 mg/day in 3-4 divided doses, increased upto a maximum of 60 mg/day.
- D/I: Same as tricyclic antidepressants.
- Cost: Not freely available.

Almitrine bimesylate

Acts on peripheral chemoreceptors

- I: Respiratory failure, CNS depression, chronic obstructive pulmonary disorders.
- C/I: Hypersensitivity
- S/E: Nausea, malaise, breathlessness, peripheral neuropathy.
- P/A: Tablet 50 mg.
- Dose: 50 mg o.d. or b.d.
- Cost: Not freely available.

Acetazolamide ☆

I: Respiratory failure, congestive cardiac failure, acute mountain sickness.

Dose: 250 - 500 mg / day

6.5 COUGH SUPPRESSANTS (Antitussives)

Can act centrally in the CNS to increase the threshold of the cough centre or can act peripherally in the respiratory tract to reduce the cough impulse.

Codeine phosphate

I: Dry unproductive cough. Cough which is hazardous or tiring - hernia, ocular surgery, cardiac disease.

Dose: Adults: 30 - 60 mg 4 - 6 h

Children : 1.5 - 2.5 mg/kg/day in 4 - 6 divided doses

Dihydrocodeine

I: Dry unproductive cough.

C/I: Hypersensitivity.

P/C: Caution if drowsiness, liver disease, dizziness occur. Caution if other medication containing opioids are used, avoid concurrent use of alcohol or other CNS depressant drugs.

S/E: Constipation, allergic reactions, physical dependence

P/A: Only combination preparations are available.

Dose: Adults : 30 - 60 mg 4 - 6 h

Children 1.5 - 2.5 mg/kg/day in 4 - 6 divided doses

D/I: Same as for codeine.

Pholcodeine

I: Dry unproductive cough.

C/I: Hypersensitivity.

P/C: Drowsiness, liver disease

S/E: Constipation, allergic reactions, physical dependence

P/A: Linctus (combination preparation)

Dose: Adults : 5 - 10 mg 4 - 6 h.

Children 1.5 - 2.5 mg/kg/ 24 hours in 4 - 6 divided doses

Cost: No pure preparations available.

Morphine sulphate ☆

I: Irritant non productive cough

Dose: 2 - 4 mg i.m.

6. Drugs used in Respiratory Diseases

Methadone

Dose : 10 - 200 mg every 2 -4 h.

Dextromethorphan ✧

Non narcotic antitussive

I: Dry or painful cough

C/I: Liver disease

P/C: Same as codeine phosphate.

S/E: Nausea, vomiting, headache

P/A: Only combinations are available.

Dose : 15 - 30 mg 4-6h

D/I: MAO inhibitors

Cost : Only combinations are available.

Benzonatate

Local anaesthetic that acts peripherally to reduce the afferent tussive impulses

I: Symptomatic treatment of non productive cough

C/I: Sensitivity to topical anaesthetics and benzonatate.

P/C: Young children, since numbness of the mouth, pharynx, and tongue may occur, which may cause swallowing difficulty and aspiration.

S/E: Dizziness, nausea, rashes, ocular irritation

P/A: Capsule 100 mg

Dose : 100 mg t.d.s.

D/I: Concurrent use with CNS depressing drugs will potentiate CNS depressing action.

Cost : Not freely available.

6.6 EXPECTORANTS

Increase bronchial secretions or reduce its viscosity.

6.6.1 Directly acting

Sodium/potassium citrate (0.3 -1 g)

Sodium/potassium acetate

Potassium iodide (0.2 - 0.3 g)

Guaiphenesin

Vasaka (2 - 4 mL)

6.6.2 Reflexly acting

Ammonium chloride

Potassium iodide

Ipecacuanha

6.7 MUCOLYTICS

Act by depolymerising mucopolysaccharides directly as well as by liberating lysosomal enzymes

Bromhexine

I: Conditions where the sputum is viscid and tenaceous.

C/I: Hypersensitivity.

P/C: Use with caution in patients with gastric ulceration.

S/E: Gastric irritation, allergic reactions, rhinorrhoea, lacrimation.

P/A: Tablet 8 mg

Syrup 4 mg/ 5 mL

Dose: 8-16 mg, t.d.s-q.d.s.

Cost: Tab 8 mg (10) Rs. 6.00 - 8.00

Syrup 4 mg/5 mL (100 mL) Rs. 20.00 - 25.00

Acetyl cystine

I: Mucolytic, diagnostic aid in bronchial studies.

C/I: Asthma, respiratory insufficiency, hypersensitivity.

P/C: Check with physician if condition worsens.

S/E: Pungent smell, irritant to the bronchial tree. Hemoptysis, increased airway obstruction, clammy skin, fever, nausea, vomiting, rhinorrhea.

P/A: Granule sachet

Nebulising solution

Dose: 200 mg b.d., 3 - 5 mL of 10 - 20% solution

Ambroxol Hydrochloride

P/A: Tablet 30 mg

Syrup 30 mg/5 mL

Drops 7.5 mg/mL

Dose: Adult - 15 to 30 mg b.d. or t.d.s.

Children - 3.75 to 7.5 mg b.d.

6.8 PULMONARY SURFACTANT

This is mainly secreted by type II alveolar cells. It is a complex mixture of lipids, proteins and carbohydrates. Main lipid is DPPC - dipalmitoyl phosphatidyl choline. Surfactant deficiency results in wide spread atelectasis, poor compliance, oedema and hemorrhage.

Surfactant Replacement Therapy. Please refer to specialised institution.

I: Hyaline membrane disease

6. Drugs used in Respiratory Diseases

ARDS

<u>Name</u>	<u>Components</u>	<u>Dose</u>
Exosurf	DPPC, acetyl alcohol Tyloxapol	5mL/kg
Survanta	Bovine lung extract DPPC, Palmitic acid Tripalmitin	4 mL/kg

6.9 OXYGEN THERAPY

Aim: To restore tissue oxygen tension towards normal by improving arterial oxygen content and subsequently to reduce the work of breathing and myocardial stress.

6.9.1 Short Term Oxygen Therapy

I: 1. Hypoventilation

- (a) Central respiratory depression : Drug overdosage, CNS injury, general anaesthesia,
- (b) Peripheral : Chest trauma, neuromuscular blockage, diaphragmatic dysfunction

2. Post operative hypoxemia :

- (a) Hypotension, shock, haemorrhage
- (b) Ischemic heart disease, reduced cardiac output
- (c) Anaemia, obesity
- (d) Hypothermia, hyperthermia, pulmonary oedema

- 3. Increased oxygen demand : convulsions, hyperthermia, shivering
- 4. Venous admixtures : asthma, COPD, pneumonia
- 5. Carbon monoxide poisoning
- 6. To reduce surgical emphysema, pneumothorax and air embolism
- 7. Ascent to high altitude
- 8. To treat hypoxia during exercise and sleep apnoea.

6.9.2 Long Term Oxygen Therapy

- I:
- 1. Advanced COPD
 - 2. Interstitial lung disease
 - 3. Cystic fibrosis
 - 4. Chronic congestive cardiac failure
 - 5. Malignancy with hypoxia

Device	Oxygen flow in L/min	Target FiO ₂
Nasal cannula	1-6	21 - 40 %
Face mask	5-10	35 - 50%
Reservoir mask (rebreathing)	5 - 15	50 - 90 %
Reservoir mask (non rebreathing)	5 - 15	50 - 90 %
Venturi	4 - 10	24 - 40 %
CPAP (Continuous positive airway pressure)	10 - 15	50 - 100 %

Colour codes of Venti masks

Colour	FiO ₂	Oxygen Flow Rate L/min
Blue	24%	2 - 4
Yellow	28%	4
White	31%	6
Green	35%	8
Calamine	40%	8 - 10
Orange	50%- 60%	10 - 15

Drug interactions of Oxygen

Catecholamines, thyroid hormones, steroids, bleomycin, cyclophosphamide and nitrofurantoin enhance pulmonary toxicity of oxygen.

Indications for hyperbaric oxygen therapy :

Hyperbaric oxygen is the administration of oxygen under higher than normal atmospheric pressure. This is effected by enclosing the patient in the high pressure chamber. This facility is available in the limited number of institutions. Hyperbaric oxygen dissolves in larger amount in plasma and so the oxygen carrying capacity of blood is increased.

1. Decompression sickness
2. Carbon monoxide poisoning
3. Clostridial myonecrosis
4. Acute ischaemia
5. Air embolism
6. Thermal Injury - burns

Side effects of Oxygen Therapy:

1. Pulmonary Oxygen Toxicity : manifested as substernal distress, cough, refractory hypoxia, Chest X-Ray shows diffuse and patchy bilateral infiltrates and alveolar atelectasis.

6. Drugs used in Respiratory Diseases

2. Retrolental fibroplasia in new born and varying exposure to high concentrations of oxygen lead to vascularisation in the eye and impairment of vision.
3. Central nervous system toxicity : twitching and convulsions.

6.10 HAEMOSTATICS

These are at times used for symptomatic relief of haemoptyses. There is no proof that these are effective and so their use is empirical.

Haemocoagulase

Isolated from venom of snakes of the species bothrops.

- I: Haemostatic in primary, secondary and post operative internal and external haemorrhage

C/I: Pregnancy (1st 3 months) and lactation.

Patients with history of thrombotic or embolic episodes.

P/C: If the solution is coloured discard the preparation.

S/E: Allergic reactions. Rarely disseminated intravascular coagulation.

P/A: Injection 1 unit/ mL

Dose: Adults : 1 amp i.m., s.c. or i.v. (if serious bleeding occurs) SOS or o.d.

Children : 1/3 or 1/2 ampoule depending on the age.

D/I: None reported

Cost: Inj1 unit/ mL Rs. 35.00-40.00

Adrenochrome

Dose: 1 - 5 mg oral or i.m.

Efficacy is uncertain.

Rutin

Plant glycoside claimed to reduce capillary bleeding.

Dose: 60 mg orally b.d. or t.d.s, Efficacy is uncertain

If moderate haemoptysis, admit the patient for observation. Treat infection if any. Do bronchoscopy. And if the haemorrhage stops, treat the underlying cause. If haemorrhage continues, consider surgical intervention : embolization, laser cautery or resective surgery. If haemoptysis is massive (> 600 mL in 24 hours or > 200 mL in 1 bout), intubate the patient to protect the airway. Foot end of the bed is elevated. Haemostatics and cough suppressants are administered. Further management is the same as for moderate haemoptysis.

6.11 ANTICOAGULANTS

6.11.1 Heparin ☆

Details are given in chapter 10

6.11.2 Oral anticoagulants

Warfarin, acenocoumarin, dicoumerol ☆

They are competitive antagonists of vitamin K

Drug	Half life	Loading dose	Maintanance dose
Dicoumarol	25 – 100 hours	200 mg for 2 days	50 - 100 mg
Warfarin sodium	36 - 44 hours	30 mg	2.5 - 10 mg
Acenocoumarin	24 hours	10 - 20 mg	2 - 10 mg
Phenindione	5 hours	200 mg	50 - 100 mg

CHAPTER 7 : DRUGS USED IN ENDOCRINE DISORDERS

7.1 DISORDERS OF GLUCOSE METABOLISM

7.1.1 Drugs used in Diabetes Mellitus

Diabetes mellitus is a metabolic disease affecting carbohydrates, protein and fat metabolism, due to absolute or relative deficiency of insulin. The major subdivisions are Type I (IDDM) Type II (NIDDM) and secondary diabetes including fibrocalculus pancreatic disease. The Type I (IDDM) is a pure endocrine disorder due to absolute deficiency of insulin and as such, its treatment includes insulin therapy along with dietary restriction. All these patients of Type I should receive insulin, otherwise they will go into ketoacidosis. Of the oral drugs only α -glucosidase inhibitor (acarbose), has only a limited role in Type I diabetes.

Type II diabetes is a heterogeneous group with varying levels of endogenous insulin. They may have insulin insufficiency or normal levels or higher circulating insulin, with insulin resistance. So the treatments of Type II may vary from diet restriction, weight reduction and exercise to oral hypoglycemic agents. Some of the Type II may require insulin therapy in addition to diet, exercise and oral hypoglycemic agents.

Diabetes developing during pregnancy is known as Gestational diabetes and requires diet restriction with or without additional insulin therapy. Known diabetic patients becoming pregnant or gestational diabetes, requiring drugs, should not be given oral hypoglycemic agents during pregnancy, only insulins.

Other types of secondary diabetes including fibrocalculus pancreatic diabetes require dietary restriction, exercise and drug treatment. There are no generalised guidelines for drug therapy of secondary diabetes, some can be controlled with oral hypoglycemic drugs and others may require insulin.

Management of diabetes includes not only dietary advice, exercise, oral drugs and insulin, but patients' education also. Without patients' active co-operation, diabetes management will not be perfect.

GENERAL PRINCIPLES

To employ measures that will help the patients to attain the best possible control of plasma glucose concentration. All patients should try to maintain ideal body weight. All diabetics should have regular exercise for at least 20 - 30 min/day. They should be very punctual with their medicine intake, food and exercise.

PRESCRIPTION OF GOOD DIABETIC DIET

There is no single recommended diabetic diet. Diet should be prescribed with commonly available foods with scope for adequate flexibility and variety.

- ♦ Energy and carbohydrate intake must be adequate to allow normal growth and development.
- ♦ The total intake must be distributed between various meals in a day.
- ♦ Recommended caloric intake.
150 KJ / kg or 36 Kcal / kg for men
140 KJ / kg or 34 Kcal / kg for women
- ♦ Recommended protein intake - 1 - 1.5 / kg/day.
If the patient has diabetic nephropathy 0.8 g / kg / day.
10 % of calories from proteins.
- ♦ The distribution of calories between fat and carbohydrates depends on whether the patient is obese or normal weight. The consumption of fat is to be reduced in the obese. 30 % of total calories should be obtained from dietary fat with less than 10 % from saturated fat. Remaining calories (60%) to be obtained from carbohydrates.
- ♦ Dietary management most important in NIDDM patients not on insulin therapy.

7.1.1.1 Oral hypoglycemic agents

7.1.1.1.1 Sulphonyl Ureas

They stimulate the release of insulin from the beta cells. Some also increases the number of insulin receptors and enhances insulin mediated, glucose transport independent of increased insulin binding.

First generation sulphonyl ureas include chlorpropamide, tolazamide, tolbutamide, acetahexamide.

Second generation sulphonyl ureas include glibenclamide, glipizide, gliclazide. Second generation drugs are effective in smaller doses and highly potent. Gliclazide may have more extrapancreatic effects especially in fibrinolytic system which is beneficial.

Indication : NIDDM (type 2) whenever dietary treatment alone proves inadequate.

Not to be used in type 1, diabetic emergencies, hypersensitivity states and pregnancy.

Tolbutamide

I: NIDDM (Type 2)

C/I: Pregnancy, Type I diabetes, diabetic ketoacidosis.

P/C: Driving vehicles or operating machinery, tolbutamide may potentiate or attenuate the effect of alcohol.

S/E: Nausea, sensation of gastric fullness, hypersensitivity, skin reactions.

7. Drugs used in Endocrine Disorders

transient changes in haematopoietic system, metabolised by liver.

P/A: Tablet 500 mg.

Dose: 500 - 3000 mg/day 1 - 3 divided doses.

If dose exceeds 1 g to be taken in divided doses or else before breakfast or of the first substantial meal.

D/I: Effect enhanced by salicylates, sulphonamides, chloramphenicol and cyclophosphamide. Effect reduced by corticosteroids, adrenaline, oral contraceptives and thiazide diuretics.

Cost: Tab 500 mg (10) Rs. 7.00 - 8.00

Chlorpropamide

I: NIDDM (Type 2), Partial cranial diabetes insipidus.

C/I: Hepatic insufficiency, renal insufficiency, cardiovascular disease, predisposing to tissue hypoxia, alcohol intoxication, pregnancy, surgery, stress.

P/C: Use with caution in renal dysfunction, congestive cardiac failure, liver disease, pancreatitis, ischemic vascular disease. May cause intolerance to alcohol.

S/E: GI upset, leukopenia, thrombocytopenia, jaundice, rashes, skin eruptions, anemia, hypoglycemia.

P/A: Tablet 100 mg, 250 mg

Dose: 100 - 125 mg o.d., gradually increased up to 500 mg o.d.

D/I: Phenobarbitone and rifampicin accelerate hepatic metabolism of chlorpropamide. Phenylbutazone and salicylates potentiate chlorpropamide. Thiazide diuretics, phenytoin and verapamil reduces insulin release by chlorpropamide.

Cost: Tab 250 mg (10) Rs. 3.00 - 4.00

Glibenclamide (Gliburide) ☆

I: NIDDM (Type 2)

C/I: Pregnancy, Type I diabetes, diabetic ketoacidosis.

P/C: Underweight individuals prone to hypoglycemia especially after unusual exercise, hypoglycemia.

S/E: Nausea, vomiting, anorexia, pruritus, urticaria, leukopenia, thrombocytopenia. Metabolised by liver/kidney

P/A: Tablet 2.5 mg, 5 mg.

Combination with metformin in varying proportion is also available.

Dose: 1.25 to 20 mg / day. Start as a single dose in the morning, the smaller doses and increase slowly.

If the requirement is more than 10 mg, then given b.d. with a major morning and smaller evening dose.

saccharides and disaccharides to monosaccharides is delayed. This will help to control post prandial hyperglycemia. There is no malabsorption, only delaying the absorption to distal ileum.

- I: NIDDM, IDDM along with insulin, reactive hypoglycemia.
- C/I: Hypersensitivity, malabsorption, intestinal obstruction, hepatic impairment, pregnancy and lactation.
- P/C: Monitor liver enzyme values periodically. If hypoglycemia occurs then give glucose orally.
- S/E: Flatulence, dyspepsia, abdominal distension and diarrhoea, anorexia, erythema, tenesmus. Occasional elevation of liver enzyme on high dose.
- P/A: Tablet 50 mg, 100 mg.
- Dose: 50 mg o.d. first week, 50 mg b.d. second week and 50 mg t.d.s. third week.
- D/I: Enhanced effect of acarbose with cholestyramine. Action of acarbose antagonised by frusemide, steroids, phenothiazines, phenytoin and isoniazid. Reduced effect with charcoal, amylase and pancreatin.
- Cost: Tabs 50 mg (10) Rs. 55.00 - 56.00

7.1.1.4 Insulins

Insulin is a polypeptide hormone playing an important role in the body's metabolism of carbohydrate, protein and fat. Defective insulin synthesis, secretion or action causes diabetes mellitus.

Insulin may be bovine, pork, or human (Recombinant DNA technology). The first two are being progressively replaced by human insulins.

Bovine insulin (differ by 3 amino acids) and pork insulins (differs by one amino acid) are extracted from pancreas and purified human insulins are synthesised either by recombinant DNA technology using escherichia coli or semi synthetically by enzymatic modification of porcine insulin. All insulin preparations especially bovine or porcine insulin are to an extent immunogenic.

Commonly available insulins come in two strengths - 40 iu/mL and 100 iu/mL. Commercial insulin are of varying purity.

- Conventional insulin : (Pro insulin like substances < 30,000 ppm.)
- Highly purified insulin : (Pro insulin like substances < 10 ppm)
- Mono component insulin : (Pro insulin like substances < 1 ppm)

Insulins of greater purity are obtained by advanced chromatographic methods and produce decline in the incidence of insulin allergy, insulin resistance and localised lipodistrophy.

INSULIN FORMULATIONS**a. Short acting insulins.**

Regular insulin : Can be given intravenously or subcutaneously or intramuscularly.

1. Conventional plain insulin (porcine or bovine)
2. Highly purified or monocomponent.
3. Human insulin.

	Maximum action	Duration
Intavenous	5 - 7 min	20 min
Intramuscular	30 - 60 min	2 - 4 h
Subcutaneous	2- 3 h	4 - 8 h

Insulin Analogues

These can be given with meals whereas regular insulin has to be given 15-20 min before meals. The commercially available insulin analogue is **Lyspro insulin** in which the two aminoacids at B28 and B29 (lysine and proline) are interchanged. This lisproinsulin is short acting insulin analogue and has the advantage of quick action within 10 - 20 min after subcutaneous injection. The incidence of late hypoglycemia is also less as the duration of action is only 3 to 4 h.

Short acting insulins are used in diabetic emergencies (diabetic ketoaciduria). At the time of surgery, during admission and acute medical illness like myocardial infarction, labour and for initial dose titration in type 1 diabetes and insulin requiring type 2 diabetes.

b. Intermediate acting insulins.☆

NPH (Neutral Protamine Hagedorn)

Lente Insulin: Onset 1.5 - 4.0 h
Peak 6 - 16 h
Duration 14 - 24 h

c. Long acting insulins

	Onset	Maximum	Duration
Ultra lente	3-8 h	4 - 10 h	9 - 36 h
ZI	3-8 h	14 - 26 h	24 - 40 h

Both Intermediate and long acting insulins are available as conventional, highly purified, mono component or Human insulin. NPH can be mixed with soluble insulin in the syringe and will retain the effects of both. Lente, though can be mixed, there might be some decrease in the effects of the soluble component. They are given as subcutaneous injection, and should never be

used intravenously. They are used further routine management of type I diabetes insulin requiring type II diabetes.

d. Pre Mixed Biphasic Insulins

Combination of soluble and NPH insulins are available as ready made mixture of various combination. The commonest and most widely used combination is 30:70 which contain 30% soluble and 70% NPH insulin. Other combination is 50:50, 25:75 etc.

A few recommended regimens

- Short acting insulin t.d.s. with intermediate acting insulin at bed time-for tight control.
- Short acting insulin mixed with intermediate acting insulin b.d. before meals-for IDDM patients
- Intermediate acting insulin with or without short acting insulins once daily either before breakfast time suffices for some NIDDM patients needing insulin.
- Intermediate acting insulin as a single bedtime dose along with day time OHAs for Type II patients, the so called basal insulin therapy.

Insulin Preparations

Regular (plain)

Conventional Bovine	40 iu	10 mL	Rs. 50.00
Highly Purified Pork	40 iu	10 mL	Rs. 110.00
Human Regular	40 iu	10 mL	Rs. 200.00

NPH (Isophane)

Conventional Bovine	40 iu	10 mL	Rs. 50.00
Highly Purified Pork	40 iu	10 mL	Rs. 110.00
Human Regular	40 iu	10 mL	Rs. 200.00

Lente

Conventional Bovine	40 iu	10 mL	Rs. 50.00
Highly Purified Pork	40 iu	10 mL	Rs. 110.00
Human Regular	40 iu	10 mL	Rs. 200.00

Premixed

Highly purified pork/beef	40 iu	10 mL	Rs. 70.00
Highly Purified Pork	40 iu	10 mL	Rs. 110.00
Human Regular	40 iu	10 mL	Rs. 200.00

7. Drugs used in Endocrine Disorders

P/C: Decrease the dose of insulin those patients with impaired renal function.

S/E: Hypoglycemia, insulin allergy

Lipodystrophy (lipoatrophy, lipohypertrophy)

Storage : Store at 2 to 8° C. Avoid freezing.

7.1.2 Drugs used in gestational diabetes

The control of diabetes has to be meticulous. Insulin alone should be used. More frequent antenatal visits are required for diabetic mothers every two weeks up to 28 weeks and weekly there after. They need be admitted only if any complication develops or as usual at term if the blood sugar is controlled.

Vast majority require insulin therapy. Insulin requirement rises slowly till term and may increase by 50 - 100 % near term. Oral hypoglycemics are contra indicated as they cause severe neonatal hypoglycemia. The plasma glucose must be ideally monitored by self monitoring (SMBG) or at least by fasting blood sugar and RBS estimation at each antenatal visit, along with estimation of Hb A1C.

7.1.3 Drugs used in acute myocardial infarction for control of diabetes.

Plasma glucose concentrations are kept within euglycemic ranges by short acting soluble insulins after frequent monitoring of blood glucose. Because of the dietary restriction in the acute stage, plasma glucose monitoring is a must. Requirements may rise due to the acute stress.

7.1.4 Diabetic nephropathy

Annual monitoring of diabetic patients for estimation of urinary protein. If absent in routine evaluation, urine should be tested for microalbuminuria.

Patient with diabetic nephropathy should have dietary protein restriction (0.8 g/kg/day). Patient with renal failure should be treated with small doses of insulin as OHAs should be avoided.

Control of blood pressure to maintain systolic B.P below 140 mmHg and diastolic below 90 mmHg. All insulin dependent patient with confirmed microalbuminuria should be treated with an ACE inhibitors. It can potentiate the hypoglycemic effect of insulin and oral hypoglycemics especially in the first weeks of combined treatment and in patients with renal impairment.

7.1.5 Diabetic neuropathy

The plasma blood glucose must be optimally controlled preferably with insulin.

Symptomatic management for the pain include non opioid analgesics like paracetamol and aspirin, tricyclic anti depressants, amitryptiline and imipramine, with or without a low dose of phenothiazine. Carbamazepine and phenytoin are also useful in some cases of severe neuropathy. Capsaicin local application may be helpful in some cases.

Antiemetics and cisapride may control vomiting in diabetic gastroparesis. Erythromycin may also be tried but should not be mixed with cisapride as they can cause dangerous arrhythmias. Codeine phosphate is an ideal drug for diabetic diarrhoea due to autonomic neuropathy but may be aborted by a course of tetracycline 250 mg 6 h for 5 days.

In postural hypotension due to autonomic neuropathy the patient should be advised to increase salt intake. Fludrocortisone 100 - 400 mcgs alone or in combinations with fluribiprofen and ephedrine hydrochloride, may be tried but can have edema as a common side effect.

7.1.6 Drugs precipitating or aggravating diabetes

Epinephrine, glucocorticoids, diuretics, diazoxide, oral contraceptives, beta 2 adrenergic agonist, calcium channel blockers, clonidine, H₂ receptor blockers, pentamidine, heparin, nalidixic acid, sulfinpyrazone, marijuana, nicotine.

7.1.7 Drugs that raise blood sugar in acute hypoglycemia

Glucagon

Polypeptide hormone produced by the alpha cells in the pancreatic islets. It mobilises glycogen from the liver and thus raising plasma glucose concentration. It may be used on an emergency basis.

I: Acute hypoglycemia

C/I: Insulinoma, phaeochromocytoma and glucagonoma, hypersensitivity.

P/C: Ineffective in chronic hypoglycemia, starvation and adrenal insufficiency.

S/E: Nausea, vomiting, diarrhoea, hypokalemia, hypersensitivity reactions.

P/A: Injection 1 mg/mL

Dose: By s.c, i.v. or i.m.

0.5 to 1 unit; if no response within 10 min i.v. glucose must be given.

D/I: Hypoprothrombinaemic effect of oral anticoagulants may be increased.

Cost: Inj 1 mg/mL (vial) Rs. 115.00 - 205.00

7.2 DRUGS ACTING AT HYPOTHALAMUS AND PITUITARY

7.2.1 Drugs acting at Hypothalamus

Anti oestrogens

This include clomiphene citrate and tamoxifen. These drugs increase the pituitary gonadotropins by blocking the oestrogen receptors at the hypothalamus. So the oestrogen feed back at hypothalamus is inhibited.

7. Drugs used in Endocrine Disorders

resulting in excess production of gonadotropins. Of these clomiphene is used mainly in inducing ovulation by increasing the pituitary gonadotropins, whereas tamoxifen is used as an antioestrogen in oestrogen sensitive breast cancers.

Clomiphene Citrate

- I: Anovulatory infertility.
- C/I: Hepatic disease, ovarian cysts, hormone dependent tumors and bleeding diathesis, neoplasm of endometrium.
- P/C: Congenital disorders of bile metabolism, infertility associated with hyperprolactinemia, and polycystic ovarian disease.
- S/E: Ovarian hyperstimulation syndrome, hot flushes, abdominal discomfort, breast tenderness, headache, nausea, vomiting, weight gain, rashes.
- P/A: Tablet 25 mg, 50 mg and 100 mg.
- Dose: 50 mg daily for 5 days, starting on the 3rd/5th day of menstruation. If no ovulation after 3 cycles, the dose must be increased to 100 mg daily for 5 days.
- D/I: In combination with gonadotropin cause hyperstimulation of ovary.
- Cost: Tab 25 mg (10) Rs. 25.00 - 30.00

Gonadorelin - (GnRH)

This is the hypothalamic gonadotropin releasing hormone, which increases the pituitary secretion of LH & FSH. It must be given intermittently to get this effect and if given continuously there will be opposite effect due to receptor saturation. This opposite effect is utilized by producing long acting analogues which are used in suppressing gonadotropin secretion in breast and prostatic cancer and endometriosis.

- I: Amenorrhoea, infertility, hypogonadotrophic hypogonadism. Also for assessing pituitary function.
- C/I: Pregnancy.
- P/C: Polycystic disease of the ovary. Treatment in women with weight related amenorrhoea should be initiated after weight correction, discontinue use if patient becomes pregnant.
- S/E: Rarely nausea, headache, abdominal pain, hypersensitivity.
- P/A: Injection 100 mcg and 500 mcg/mL.
- Dose: For amenorrhoea and infertility : initially 10 - 20mcg over 1 min repeated every 90 min by s.c. or i.v. pulsatile infusion. This can be continued upto 6 months.
For assessing pituitary function : 100 mcg i.v. bolus.
- D/I: Spironolactone and levodopa stimulates gonadotropin secretion while phenothiazines, dopamine antagonist, digoxin and sex hormones can inhibit gonadotropin secretion.
- Cost: Not freely available.

Gonadorelin analogues

Buserelin

- I: Prostatic cancer, endometriosis.
- C/I: Pregnancy, breast feeding.
- P/C: Polycystic disease of the ovary.
- S/E: Menopause like syndrome, migraine, vaginal bleeding.
- P/A: Injection 1 mg/mL.
Nasal spray 10 mg multidose container(100 doses)
- Dose: 500 mcg s.c. every 8 h for 7 days followed by 100 mcg nasal spray 4 h on the following days.
- D/I: Same as for gonadorelins.
- Cost: Not freely available.

Thyrotropin Releasing Hormone (TRH)

Protirelin

- I: For assessing thyroid function and pituitary thyrotropin (TSH) reserve.
- C/I: Pregnancy, lactation.
- P/C: Cardiac insufficiency, obstructive airway disease, severe hypopituitarism.
- S/E: Flushing, dizziness, desire to micturate, rarely bronchospasm.
- P/A: Injection 100 mcg/mL.
- Dose: By i.v. 200 mcg bolus.
For children 7 mcg/kg i.v.
- D/I: Adrenocorticoids, aspirin, levodopa and thyroid hormones may decrease the TSH response to protirelin administration.
- Cost: Not freely available.

Growth Hormone Releasing Hormones (GHRH)

Sermorelin, Somatorelin

- I: This is for assessing the pituitary growth hormone reserve.
- C/I: Pregnancy and breast feeding.
- P/C: Chronic administration causes antibody formation.
- S/E: Flushing and pain at injection, allergic reactions, obesity, hyperglycemia and elevated plasma fatty acid generation, nausea, vomiting, headache, paleness.
- P/A: Injection 50 mcg.
- Dose: By i.v. 1 mcg/kg bolus.

7. Drugs used in Endocrine Disorders

D/I: Concurrent use with clonidine, levodopa and insulin produces transient rise in somatotropin levels. Muscarinic antagonists and propyl thiouracil blunt response to sermorelin.

Cost: Not freely available.

Corticotrophin - Releasing Hormone (CRH)

CRH is a 41 amino acid peptide hormone synthesized by the neurons in the hypothalamus. It stimulates release of ACTH and endorphins.

I: To differentiate between Cushing's disease and ectopic ACTH syndrome.

Assess the success of operation in Cushing's disease.

Cause of adrenal insufficiency can be determined, whether hypothalamic or pituitary.

S/E: i.v. bolus can produce transient facial flushing and rarely dyspnoea and hypotension.

P/A: Both human and sheep CRH available. Injection 100 mcg.

Dose: Dosage 1 mcg/kg. To be dissolved in water not saline.

Cost: Not freely available

7.2.2 Drugs acting at pituitary

7.2.2.1 Anterior Pituitary Hormones

ACTH - Adrenocorticotrophin

ACTH is a 39 amino acid peptide produced by anterior pituitary. It stimulates the adrenal cortex to produce cortisol. It is released in pulses with an overriding circadian rhythm.

I: Diagnosis of primary and secondary adrenal insufficiency (24 hour ACTH infusion and rapid ACTH stimulation test), differentiate between late onset congenital adrenal hyperplasia from states of ovarian hypo gonadism in women with hirsutism, therapeutic use in treatment of infantile spasm. Can be used as alternative to glucocorticoids but is inferior.

C/I: In pregnancy, similar to glucocorticoids.

P/C, D/I: Same as for corticosteroids

S/E: Anaphylactic reactions, refractoriness due to antibodies developed, painful at the site of injection and side effects of glucocorticoids.

P/A: Porcine ACTH & Human ACTH (cosyntropin) 1 unit of Porcine ACTH = 10 mcg of cosyntropin

Dose: Therapeutic - 10 - 20 units 6h, i.m.

Respository ACTH- 40 - 80 units every 24 - 72 hrs.

Cost: Inj 60 iu/mL (5 mL) Rs. 850.00

Tetracosactrin

I: For testing adrenocortical function and the differential diagnosis of diseases of the adrenal cortex. Previously it was used as an alternative to corticosteroids. To stimulate adrenal cortex while withdrawing high dose corticosteroids used on a long term basis.

S/E: Anaphylaxis.

P/A: Injection 20, 40, and 80 units/mL

Dose: Inj Tetracosactrin 250 mcg as a single dose i.m./i.v for short tests.
For 5 h prolonged tests use 1 g depot preparation as i.m. injection.

D/I: None reported.

Cost: Not freely available.

Gonadotropins

Gonadotropins include luteinising hormone (LH) and follicle stimulating hormone (FSH) which are secreted by anterior pituitary gland. These are used for treating hypogonadotropic hypogonadism in both males and females and also for inducing ovulation where clomiphene do not work or during superovulation assisted conception. Chorionic gonadotropin which has got L.H. property is also used for undescended testes and for initiation of pubertal changes in cases of delayed puberty.

Human Chorionic Gonadotropin (HCG)

It is obtained from urine of pregnant women and has action as pituitary LH.

I: Hypogonadotropic hypogonadism, ovulation induction, delayed puberty and undescended testes.

C/I: Allergy to leutinising hormone (LH), pregnancy, lactation.

P/C: Chronic hepatic and renal dysfunction, epilepsy, migraine, asthma and cardiac disorders.

S/E: Oedema, headache, tiredness, ovarian hyperstimulation, multiple pregnancy, gynaecomastia.

P/A: Injection 500, 1000, 1500, 2000, 5000 and 10000 iu.

Dose: i.m. or s.c. 1500 - 5000 units three times weekly.

D/I: No known interactions

Cost: Inj 1000 iu (3 ampoules) Rs. 390.00 - 575.00

Follicle stimulating hormone (FSH) - Urofollitropin

Produced from the urine of post menopausal women.

I: Hypogonadotropic hypogonadism, ovulation induction, spermatogenesis stimulation.

C/I: Abnormal vaginal bleeding, ovarian cyst or enlargement not associated with polycystic ovary syndrome.

P/C: Ovarian cyst, intracranial lesions, adrenal and thyroid disorder.

7. Drugs used in Endocrine Disorders

S/E: Ovarian hyperstimulation, local reaction, multiple pregnancy.

P/A: Injection 75 and 150 units (powder for reconstitution with solvent).

Dose: By s.c. or i.m. 75 units daily / 3 times weekly.

D/I: None reported.

Cost :75 iu (1 ampoule) Rs. 660.00 - 665.00

Human Menopausal Gonadotropins

Contain both LH and FSH obtained from menopausal urine.

I: Hypogonadotrophic hypogonadism, ovulation and spermatogenesis induction.

C/I: Abnormal vaginal bleeding, ovarian cyst not associated with polycystic ovarian syndrome.

P/C: Ovarian cysts, should not be given to pregnant patients.

S/E: Ovarian hyperstimulation, multiple pregnancy

P/A: Injection 5 units FSH + 75 units LH (powder for reconstitution supplied with solvent)

Dose: i.m. injection 75 units FSH + 75 units LH daily to 3 times weekly.

D/I: None reported.

Cost : Inj 75 units FSH + 75 units LH Rs. 260.00 - 575.00
(powder for reconstitution supplied with solvent)

Growth Hormone (GH) - Somatropin

Prepared by recombinant DNA technology and is the hormone for replacement in growth failure due to pituitary GH deficiency.

I: Growth hormone deficiency, short stature, in Turner's syndrome to improve height.

C/I: Evidence of tumour activity especially pituitary or intracranial tumors as there may be recurrence of tumour. Patients with closed epiphyses.

P/C: Diabetes mellitus.

S/E: Fluid retention, hypothyroidism, arthralgia, myalgia.

P/A: Injection 4, 12, 16 units (powder for reconstitution supplied with solvent)

Dose: By s.c. dose of 0.1 unit/kg/day to be increased as per clinical response.

D/I: Antagonises insulin.

Cost : Inj 4 units (1 vial) Rs. 1800.00

7.2.2.2 Posterior Pituitary Hormones

The two main hormones secreted by posterior pituitary are vasopressin and oxytocin. Of these vasopressin and its analogues are used in the management of cranial diabetes insipidus, as an emergency measure to reduce

portal hypertension, to improve the coagulation defects in milder forms of haemophilia and Von Will Brand's disease. Oxytocin is mainly used in obstetrics and is discussed separately.

Vasopressin (Antidiuretic hormone - ADH)

ADH is a peptide hormone released from the posterior pituitary in response to a falling plasma tonicity or falling blood pressure. It is a non peptide and acts via V_1 Receptor (vascular smooth muscle) and V_2 Receptors (renal tubule). Half life is less than 20 minutes.

- I: Pituitary diabetes insipidus and bleeding from oesophageal varices.
- C/I: Coronary artery disease or any other occlusive arterial disease, chronic nephritis if blood urea nitrogen levels are high.
- P/C: Pregnancy, heart failure, migraine, renal impairment, epilepsy, in conditions associated with fluid overload, with cautions in patients with coronary artery disease, asthma and epilepsy.
- S/E: Pallor, nausea, abdominal cramps, desire to defecate, belching, hypersensitivity reactions, anginal attacks.
- P/A: Injection 20 iu/mL (aqueous vasopressin, vasopressin tannate in oil and lysine vasopressin).
- Dose: s.c or i.m. (for diabetes Insipidus) 5 - 20 units/4 hrs.
By i.v. infusion for the initial control of variceal bleeding 20 units given over 15 minutes is ideal.
- D/I: Carbamazepine, chlorpropomide may enhance the anti diuretic effect of vasopressin, demeclocycline, lithium, heparin and alcohol may decrease antidiuretic action of vasopressin.
- Cost: Inj 20 iu/mL (1 mL) Rs. 130.00 - 131.00

Desmopressin

Has less pressor activity than vasopressin and hence is preferred in Diabetes insipidus.

- I: Diabetes insipidus
- C/I: Cardiac insufficiency and other conditions treated with diuretics.
- P/C: Renal impairment, cardiovascular disease, elderly (> 65)
- S/E: Same as vasopressin.
- P/A: Injection 4 mcg/mL
Nasal spray / solution 0.1 mg/mL.
- Dose: Intranasal: Diabetes insipidus.
Adult - 10 - 40 mcg/day in divided doses.
Child - 5 - 20 mcg/day in divided doses.
Parenteral: Diabetes insipidus.
Adult - 1- 4 mcg daily

7. Drugs used in Endocrine Disorders

Child - 400 nanograms.

Also given for primary nocturnal enuresis.

D/I: Same as for vasopressin.

Cost: N.Spray/solution 0.1 mg/mL (2.5 mL) Rs. 1130.00 - 1140.00

Inj 4 mcg / mL (10 x 1 mL) Rs. 710.00 - 725.00

Lypressin

Vasopressin analogue.

I, C/I, S/E : Same as desmopressin.

P/C : Sensitivity to vasopressin.

P/A : Injection 23.4 mcg/ampoule (approximately 7.7 units)

Nasal solution 0.185 mg/mL (approximately 50 units)

Dose : i.v. 5 - 10 units t.d.s.

D/I: Same as for vasopressin.

Cost : Not freely available

Terlipressin

Vasopressin analogue

I : Bleeding oesophageal varices.

C/I :, P/C:, S/E : Same as for vasopressin.

P/A : Injection 1 mg (powder for reconstitution)

Dose : 2 mg i.v. followed by 1 - 2 mg 4 - 6 h.

D/I: Same as for vasopressin.

Cost : Not freely available.

7.3 DRUGS FOR THYROID DISORDERS

Basically thyroid diseases can be classified as hyperthyroid conditions and hypothyroid conditions. The former can be treated either with drugs or by medication using radioactive iodine. Symptomatic relief can be produced by other drugs such as sedatives, beta adrenergic blockers and the like. Hypothyroidism has to be treated by supplementation of thyroid hormones.

7.3.1 Management of Hypothyroidism

The essential part of therapy is thyroid hormone supplementation.

Thyroid Hormone

Thyroid hormone supplementation is absolutely essential for proper growth, development, metamorphosis and maintenance of normal health. Institution of thyroid supplementation therapy should be done without any

delay in younger children, and in new borns with hypothyroidism since any delay in treatment during this period of life will result in long term defects in mental faculties. Thyroid hormone supplementation is also used as a form of suppressive therapy since it inhibits TSH production and thereby reduces further growth of thyroid. Synthetic thyroxine sodium (T_4) is the commonest preparation used for replacement therapy. Tri-iodo-thyronine is available as liothyronine sodium, abroad and is specially indicated in situations like myxoedema coma where you require rapid action. Dried thyroid extract was in vogue but they are not recommended.

Thyroxin Sodium (T_4)

I: Hypothyroidism - primary and secondary, suppressive therapy in non toxic goitre, thyroid cancer and hashimotos thyroiditis.

C/I: Thyrotoxicosis, hypersensitivity.

P/C: In hypothyroidism secondary to hypopituitarism, thyroid supplementation to be started after corticosteroid therapy initiation. In patients with cardiovascular diseases and ischemic heart diseases start with very low dose.

S/E: Arrhythmias, anginal pain, insomnia, loss of weight, headache, flushing, excitability.

P/A: Tablet (levothyroxine sodium) 0.025, 0.05, 0.1 and 0.2 mg

Dose: Start with single daily dose of 50-100 mcg and slowly increase to 100-200 mcg on an empty stomach.

D/I: Enhances effect of anticoagulants, amiodarone elevates thyroxine level, effect of TCAs enhanced.

Cost:Tab 100 mcg (100) Rs. 18.00 - 25.00

Tri-iodo-thyronine (T_3)

This preparation is available on special request. It has much faster action than T_4 and in some situations of myxoedema coma this has to be used as life saving drug.

Dose : Oral, 10 - 20 mcg daily in divided doses.

Parenteral, 5 - 20 mcg 12 h.

Note : Eventhough thyroid hormone is the main stay of hypothyroid condition, sometimes other drugs may also have to be used. These include general supportive treatment, mood elevators, antihypertensive drugs, drugs for lowering cholesterol and others.

7.3.2 Drugs used for Hyperthyroidism

Antithyroid drugs

These are the drugs used to control thyrotoxicosis and these act by

7. Drugs used in Endocrine Disorders

interfering with the steps in thyroid hormone synthesis. The most commonly used drug in our country is carbimazole. The other drug which is equally effective is propyl thiouracil. In addition to blocking thyroid hormone synthesis they may also have a antiimmunological effect. Propyl thiouracil in addition prevents the peripheral conversion of T_4 to T_3 and so has an edge over carbimazole.

Carbimazole ☆

- I: Hyperthyroidism
- C/I: Tracheal obstruction, blood disorders.
- P/C: Liver disorders, pregnancy, breast feeding. Patient should report development of sore throat, mouth ulcer, rash, etc. indicative of abnormalities in blood.
- S/E: Nausea, vomiting, rashes, pruritis, arthralgia, hepatitis, agranulocytosis.
- P/A: Tablet 5 mg, 10 mg and 20 mg.
- Dose: Starting dose 15 - 60 mg / day
Maintenance 5 - 15 mg/day.
- D/I: Increased sensitivity to warfarin in hyperthyroidism.
- Cost: Tab 5 mg (100) : Rs. 21.00 - 82.00

Propyl thiouracil

- I: Hyperthyroidism.
 - C/I: Hypersensitivity, pregnancy, lactation.
 - P/C: Same as for carbimazole.
 - S/E: Fever, leukopenia, agranulocytosis, peripheral neuropathy, nephritis, renal vasculitis, changes in menstrual period, headache, nausea and vomiting.
 - P/A: Tablets 50 mg, 100 mg
 - Dose: Hyperthyroidism - 300 to 900 mg/day in divided doses till patient becomes euthyroid.
Maintenance - 50 to 600 mg/day in divided doses.
 - D/I: Decreased response to propyl thiouracil on concomitant use with iodine or potassium iodide, response to oral anticoagulants may be decreased, increased risk of digitalis toxicity.
- Note : Though anti thyroid drugs are specific agents to reduce the levels of circulating thyroid hormones, other auxillary treatment are often required since the oral antithyroid drugs produce their full effect only within 2 - 3 weeks. Tachycardia and cardiac irritability can be controlled by propranolol in a dose of 10 - 40 mg/day orally. Anxiety and excitement can be controlled by anxiolytic drugs like diazepam. In atleast a few cases hyperthyroidism is associated with abnormalities of serum potassium. This has to be monitored and appropriate steps taken. Hyperthyroidism may be associated with myasthenic reactions.*

Cost : Not freely available.

Iodides

Dietary iodine (150 - 250 mcg/day) is absolutely necessary for synthesis of thyroid hormone. A normal diet supplies this quantity. Pharmacological dose of iodide (60 - 100 mg/day) produces sudden rapid blocking action on thyroid synthesis and therefore iodides give rise to abrupt cessation of symptoms of thyrotoxicosis. They also make the thyroid gland less vascular and less friable during surgery.

Medicinal iodides

These include sodium or potassium iodide and Lugol's iodine.

Radioactive Iodine

Of all the isotopes available in clinical medicine the greatest use has been with ^{131}I . Radioactive iodine ^{131}I solution can be used for the management of thyrotoxicosis. This is very simple form of therapy, but requires facilities for handling radio active substance.

I: Investigation of thyroid disorders, treatment of hyperthyroidism not suitable for drug therapy, treatment of thyroid carcinoma. It is also indicated when hyperthyroidism has persisted or recurred after sub total thyroidectomy and when prolonged treatment with anti thyroid drugs has not led to remission.

C/I: It is contraindicated in pregnancy, but when all other forms of therapy has failed it becomes a necessity.

P/C: Not to be given to patients with nodular goitre or severe thyrotoxic heart disease.

S/E: Induction of delayed hypothyroidism.

P/A: These drugs are not to be used by general physicians. They have to be used by specially trained staff in centres which are approved by Nuclear Medicine Committee, Department of Atomic Energy, Government of India. In Kerala state this facility is available at present only in the Regional Cancer Centre, Thiruvananthapuram, though the infrastructure facilities are available at Medical College, Calicut, where the services are not yet started.

Dose : Therapeutic doses vary from person to person and depend on the weight of the gland. It should provide 7000 - 10,000 rads / gram of tissue. Usual optimal dose is 80 - 150 micro curie/gram of tissue which comes up to 4 - 10 millicurie. It is generally desirable to wait for 3 months before deciding on the necessity of a second dose.

Diagnostic uses: tracer doses of ^{131}I or ^{123}I (50 microcurie) can be used to define thyroid nodules as hot or cold, in finding ectopic thyroid tissue and occasionally metastatic thyroid tumours.

7.3.3 Drugs used in treatment of thyroid cancers

7. Drugs used in Endocrine Disorders

Medical therapy is usually combined with surgery to achieve a high cure rate. The post operative care of different thyroid cancer (DTC) include TSH suppression with levothyroxine (T_4), radio active I_2 (RAI) ablation of thyroid remnants. Surveillance RAI remnant ablation may be performed on an OP basis using upto 30 micro curie of ^{131}I or on an IP basis using 100 - 150 micro curie.

TSH suppression using T_4 is aimed at achieving a clinically euthyroid patient with low or undetectable serum TSH and normal or only slightly elevated serum T_4 . The starting dose of T_4 (Levothyroxine) is 0.1 mg/day for smaller and older patients and 0.15 mg/day for larger and younger patients. Metastases are treated with surgical or RAI ablation. Complete responses to RAI are more likely with pulmonary than osseous metastases.

Calcitonin

Calcitonin is a hormone produced by 'C' cells of thyroid gland. It is involved with parathyroid hormone in regulating the serum calcium and bone turnovers. The main action of calcitonin is to reduce the postprandial rise of serum calcium. It is used in treating hypercalcemic emergency and also for controlling pain in Paget's disease. In osteoporosis it will help to increase the bone mass and also relieve the pain. The presently used preparation is the synthetic salmon calcitonin.

- I: Hypercalcemia, Paget's disease, osteoporosis.
- C/I: Pregnancy and lactation, history of allergy to proteins, hypersensitivity.
- P/C: Calcium and Vitamin D restriction, including analogues, in patients with hypercalcemia.
- S/E: Nausea, vomiting, flushing, tingling of hands, unpleasant taste, diarrhoea, loss of appetite.
- P/A: Injection 0.5 mg (human calcitonin)
100 iu/mL (salmon calcitonin)
- Dose: Human calcitonin : 0.5 mg daily or thrice weekly s.c.
Salmon calcitonin : 4 iu/kg 12 h, increased to 8 iu/kg 12 h
(maximum 8 iu/kg 6 h)
- D/I: Concurrent use with calcium containing preparations or Vitamin D antagonises the effect of calcitonin.
- Cost : Salmon calcitonin 100 iu/mL (1 vial) Rs. 141.00 - 170.00
Human calcitonin : Not freely available.

7.4 DISEASES OF THE PARATHYROID

Hyperparathyroidism

1. Primary, due to hyperplasia or neoplasia of the parathyroid gland.

2. Secondary, occurring in chronic renal disease.

Hypoparathyroidism

1. Primary, due to autoimmune parathyroid gland atrophy.
2. Secondary, due to accidental surgical ablation or deliberate parathyroidectomy.
3. Pseudohypoparathyroidism.

Parathyroid gland produces parathormone which controls calcium homeostasis by its action on kidney, bone and intestine. It helps the metabolic conversion of vitamin D into the active form; resorption of calcium from bone and induces hypercalciuria; helps elimination of phosphates by the renal tubules. Hyperparathyroidism is characterised by hypercalcemia, hypercalcuria and bone demineralization. Hyperparathyroidism is treated by surgical excision of effected glands while hypoparathyroidism which leads to hypocalcemia and tetani is treated by calcium and vitamin D supplemetation.

Calcium and its Salts

Several preparations are available that can raise systemic concentration of calcium

- I: Used in treatment of deficiency states and as a dietary supplement when intake is inadequate. Used in severe manifest tetany, hyperkalemia.
- C/I: Calcium chloride is contra indicated in the treatment of hypocalcemia of renal insufficiency.
- P/C: Most of the preparations available for parenteral use should be used only intravenously as there is a high chance of necrosis or local abscess if used intramuscularly.

P/A & Dose :

1. Calcium chloride contains 27 % calcium usually given slow i.v. in a concentration of 10% (equivalent to 1.36 mEq calcium / mL).
2. Calcium gluceptate injection (18 mg or 22 % calcium 0.9 mEq calcium /mL)
Given as 5 - 20 mL for severe tetany.
Can also be given as 5 mL i.m. injection.
3. Calcium Gluconate 9 % Calcium.
Oral calcium gluconate tablets available as 500, 650, 975 or 1000 mg
For iv injection administered as 10 % solution (0.45 meq calcium /mL)
4. Calcium lactate (13 % calcium.)
Oral 325 or 650 mg
Also i.v. preparation.
5. Calcium carbonate available as a powder containing 40 % calcium
Available in tablets containing 350 mg to 1.5 g capsules and

7. Drugs used in Endocrine Disorders

suspensions.

6. Dibasic calcium phosphate orally powder
7. Calcium levulinate (13% calcium) orally or parenterally.
8. Calcium glubionate (6.5 % calcium).

Available as a syrup containing 1.8 g (115 mg of calcium) per 5 mL.

Vitamin D Derivatives

The drugs coming under this category includes ergocalciferol (D_2), cholecalciferol (D_3) and 1, 25-dihydroxy cholecalciferol. The Vitamin D acts mainly on the intestine to increase the intestinal absorption of calcium necessary for bone deposition activity by osteoblasts. For simple deficiency calceferol tablets of 400 units per day is enough, while for malabsorption higher doses like 40,000 units and for hypoparathyroidism doses upto 1,00,000 units per day are required. In conditions of hypocalcemia associated with chronic renal disease, since 1 hydroxytation is defective, 1 alpha cholecalciferol or 1,25 dihydroxy cholecalciferol should be used.

Ergocalciferol and Cholecalciferol

I: Hypocalcemia, nutritional, pregnancy, lactation.

C/I: Hypercalcemia.

S/E: Overdosage - nausea, vomiting.

Dose: 1.25 to 5 mg (50,000 - 2,00,000 units)/day.

Dihydrotachysterol

It is a pure crystalline compound obtained by reduction of Vitamin D

I: Hypoparathyroidism

C/I: Pregnancy, lactation, hypercalcemia, hypervitaminosis D, renal osteodystrophy with hyperphosphatemia, hypersensitivity.

P/C: Use with caution in children.

S/E: Constipation, diarrhoea, dryness of mouth, increased thirst and urination, loss of appetite, nausea, vomiting, lethargy, itching, irregular heart beat, muscle pain and pancreatitis.

P/A: Tablet 125 mcg, 200 mcg, 400 mcg.

Capsule 125 mcg.

Solution 200 mcg/mL.

Dose: Adult : 0.75 to 2.5 mg/day for several days (maintenance - 0.2 mg/day)

Child : 1 to 5 mg/day for 4 days, then decreased to one-fourth the dose if required (maintenance 0.5 to 1.5 mg/day)

D/I: Increased potential for toxicity with other Vitamin D analogues; hyperphosphatemia with phosphorous containing preparations; hypercalcemia due to the drug potentiates digitalis toxicity; reduced absorption of drug by mineral oil, cholestyramine or colestipol;

increased risk of hypercalcemia with thiazide diuretics; antagonises calcitonin, etidronate or plicamycin in the treatment of hypercalcemia; hydantoin, barbiturates or primidone accelerates metabolism of drug by hepatic microsomal drug induction.

Cost: Not freely available.

1,25 dihydroxy Cholecaliceferol (Calcitriol)

I: Hypocalcemia of malabsorption, CRF and hypoparathyroidism.

Dose: Hypocalcemia : Adult : 0.25 - 2.0 mcg/day, oral.

Child : 0.04 - 0.08 mcg/kg/day.

Mithramycin (Plicamycin)

Dose: 25 mcg/kg/day by i.v. infusion for 3 to 4 days. This drug is very effective and works in 24 to 48 h in reducing calcium levels.

Bisphosphonate

These are groups of drugs which inhibit calcium mobilization from bone. It include etidronate and alendronate.

Sodium Etidronate

I: Hypercalcemia of malignancy, Paget's disease of bone.

C/I: Hypersensitivity, pregnancy, hypercalcemia, cardiac failure, enterocolitis, hyperphosphatemia, hypocalcemia or hypovitaminosis D, impaired renal function.

P/C: Careful monitoring of fluid and electrolyte status in elderly since they are more prone to overhydration with etidronate. Use with caution in children.

S/E: Bone pain or tenderness, osteomalacia, diarrhoea, nausea, urticaria.

P/A: Tablet 200 mg, 400 mg.

Injection 50 mg/mL.

Dose: Hypercalcemia : Oral - 20 mg/kg/day for 30 days (maximum 90 days)

Parenteral : i.v. infusions at a dose of 7.5 mg/kg in 250 mL of isotonic saline over atleast 2 hours, usually given for 3 consecutive days.

Paget's disease : 5 mg/kg/day as single dose orally for 6 months.

Patients should be well hydrated and loop diuretic can also be given.

D/I: Absorption of oral etidronate prevented by antacids, milk, dairy products as well as by calcium, iron, magnesium and aluminium containing preparations.

Cost: Not freely available.

Alandronate Sodium

7. Drugs used in Endocrine Disorders

I: Post menopausal osteoporosis.

C/I: Hypocalcemia, hypersensitivity, oesophageal abnormalities, severe renal failure insufficiency, and completely bedridden.

P/C: Vit D and calcium deficiency if present should be corrected before alendronate therapy.

S/E: Dysphagea, heartburn, abdominal pain, oesophageal ulcers, flatulence, headache, rash, erythema.

P/A: Tablets 10 mg

Dose: 10 mg o.d. in the morning 30 min before breakfast with full glass of water.

D/I: Calcium supplements and antacids decrease absorption, and aspirin increases GI sideeffects. Mineral water, coffee, tea and orange juice decrease drug absorption

Cost: Not freely available.

7.5 ADRENAL HORMONES

The adrenal hormones are steroids synthesized from cholesterol derived from the diet. The main groups of hormones are glucocorticoids (cortisol), mineralocorticoids (aldosterone) and adrenal androgens (dehydroepiandrosterone) each produced in a specific zone of the cortex. At present all the available adrenal hormones are synthetic. Table shows the different adrenal hormones available for therapy.

Agent	Anti Inflammatory potency	Salt retaining potency	Equivalent Oral dose (mg)	Forms available
<u>Short medium acting glucocorticoids.</u>				
Hydrocortisone	1	1	20	O, I, T
Cortisone	0.8	0.8	25	O, I, T
Prednisolone	5	0.3	5	O, I, T
Prednisone	4	0.3	5	O
Methyl Prednisolone	5	0	4	O, I, T

Intermediate acting glucocorticoids

Triamcinolone	5	0	4	O, I, T
Paramethasone	10	0	2	O, I

Long Acting

Glucocorticoids

Betamethasone	25 - 40	0	0.75	O, I, T
Dexamethasone	30	0	0.75	O, I, T

Mineralo Corticoids

Fludrocortisone	10	125	2	O, I, T
Deoxy corticosterone acetate	0	20	-	I, P

O: Oral, I: Injectable, T: Topical, P: Pellets

P/C: Pregnancy, diabetes mellitus, osteoporosis, glaucoma, myastheniagravis, hypertension, congestive cardiac failure, renal insufficiency.

S/E: Mineralocorticoid : Sodium and water retention. Potassium loss, hypertension.

Glucocorticoid :Diabetes, osteoporosis which may lead to fractures, avascular necrosis of femoral head, mental disturbances in the form of depression, paranoid state or euphoria, peptic ulceration, proximal myopathy, iatrogenic Cushing's syndrome and suppression of growth. High dosage given for prolonged duration in pregnancy may affect development of foetal adrenals and leads to hypoadrenal state. Tissue inflammatory reactions are suppressed and so steroid therapy may mask the signs of chronic infection and delay wound healing.

Adrenal atrophy caused by prolonged therapy with corticosteroids may persist for years after withdrawing the drug. Any stressful situation like illness, surgery demand reintroduction of corticosteroid therapy, for the first year ater stopping.

7.5.1 Replacement therapy for adrenocortical insufficiency

Glucocorticoids :

Hydrocortisone : 20 - 30 mg/day with food.

15 to 20 mg morning (8.00 am)

5 to 10 mg evening (4.00 pm)

Mineralocorticoid : 0.05 to 0.1 mg of fludrocortisone orally daily.

Recommended sodium Intake = 3 - 4 g/day.

Special requirements

1. During times of stress like intercurrent illness, surgery or dental extraction the dose of gluco corticoid is increased to 75 - 150 mg/day.

7. Drugs used in Endocrine Disorders

2. Increase the dose of fludrocortisone and add salt during periods of strenuous exercise with sweating, extremely hot weather and with gastro intestinal upsets.
3. After the stress the increased doses are tapered by 20 - 30 % daily.
4. Parenteral mineralocorticoid administration is unnecessary, at hydrocortisone doses > 100 mg.

7.5.2 Adrenal Crisis

7.5.3 Cushing's Syndrome

Drug treatment depends on the cause.

a. Cushing's Syndrome due to adrenal neoplasm

In Cushing's Syndrome due to adrenal neoplasm the excision of tumour is indicated. The principal drugs for treatment of adenocortical carcinoma is mitotane (o.p¹- DOD). It is relatively selective for glucocorticoid secreting zone of the adrenal cortex.

Mitotane

- I: Inoperable functional and non-functional adrenal carcinoma and Cushing's syndrome.
- C/I: Impaired liver function, hypersensitivity, trauma or shock.
- P/C: Should not take charge of machinery or vehicles while on drug.
- S/E: Anorexia, nausea, vomiting, lethargy, somnolence, dizziness, postural hypotension, adrenocortico insufficiency.
- P/A: Tablet 500 mg
- Dose: Dose gradually increased to 8 - 10 g daily given in divided doses.
- D/I: It impairs the efficacy of administered corticosteroids, additive CNS depressant effect with CNS depression producing drugs.
- Cost: Not freely available.

b. Cushing's Syndrome due to bilateral adrenal hyperplasia

The ideal treatment for ACTH or CRH producing tumours, whether pituitary or ectopic is surgical removal. If surgical excision is not possible (especially in ectopic ACTH tumours) then either medical or surgical adrenalectomy may correct the hypercortisolism. The patients will have to be given life long mineralocorticoid and glucocorticoid replacement.

If surgery is not feasible medical adrenalectomy can be achieved by ketaconazole.

200-600 mg/day, mitotane 2 - 3 mg/day, aminoglutethimide 1 g/day or metyrapone 2 - 3 g / day.

7.5.4 Congenital adrenal hyperplasia

Gender assignment should be based on the chromosomal and gonadal sex.

Treatment with appropriate glucocorticoids stops the rapid virilization and prevents premature somatic and epiphyseal maturation. In males replacement therapy results in suppression of the abnormally elevated androgens which normalises gonadotropic secretion allowing proper testicular development and spermatogenesis. If the 21-hydroxylase deficiency is severe enough to cause excessive salt loss or elevated plasma renin activity then mineralocorticoid treatment is indicated.

Metyrapone

Metyrapone is a competitive inhibitor of 11 β -hydroxylation in the adrenal cortex. This blocks the production of cortisol and to a lesser extent aldosterone leading to an increase in the production of ACTH. This causes increased synthesis and release of cortisol precursors.

I: Differential diagnosis of ACTH - dependant Cushing's syndrome, management of Cushing's syndrome, resistant oedema due to increased aldosterone secretion in cirrhosis, nephrosis and congestive heart failure

C/I: Adrenocortical insufficiency, pregnancy and breast feeding.

P/C: Gross hypopituitarism, hypertension on long term administration, hyperthyroidism or hepatic impairment.

S/E: Nausea, vomiting, dizziness, headache, hypotension, sedation, abdominal pain, allergic skin reactions, hypoadrenalism, hirsutism.

P/A: Tablet 250 mg

Capsule 250 mg.

Dose: 1. Differential diagnosis of ACTH - dependant Cushing's syndrome - 750 mg every 4 hrs for 6 doses.

2. Management of Cushing's syndrome : 0.25 - 6 g daily.

3. Resistant oedema due to increased aldosterone secretion in cirrhosis, nephrosis and congestive heart failure - 3 g daily in divided doses.

D/I: Phenytoin increases metabolism of metyrapone. Therefore double dose of metyrapone must be given.

Metyrapone increases metabolic clearance rate of hydrocortisone.

Cost: Not freely available.

7.6 SEX HORMONES

This can be discussed under 3 headings

1. Female sex hormones.
2. Male sex hormones and antagonists.
3. Anabolic steroids.

7.6.1 Female sex hormones

Oestrogens and Progestogens are the two important group of drugs under this category.

7.6.1.1 Oestrogens

Female hormones are secreted mainly by ovaries. They are also synthesized in the peripheral tissues from circulating androgen precursors. Oestrogens are necessary for the normal development of female secondary characters and also essential for maintaining normal ovulation and menstruation. For oestrogen therapy we have naturally occurring oestrogens like oestradiol, oestrone and oestriol and synthetic oestrogens like ethinyl oestradiol, mestranol and stilbestrol. Conjugated oestrogens are available which are similar to natural oestrogens.

Oestrogen therapy is used in many gynaecological conditions including hormone replacement therapy (HRT) and contraception. It can be given cyclically or continuously. If oestrogen is given on a long term basis in patients with uterus, a progestogen should be added to prevent cystic hyperplasia of the endometrium and possible endometrial cancer. Oestrogens are no longer used for suppressing lactation as better drugs like bromocryptine are available. Thromboembolism is associated with oestrogen therapy and so in persons with history or predisposition to thrombosis, it must be used with caution.

Hormone Replacement Therapy (HRT)

Cessation of menstruation with associated decreasing hormonal production by ovaries leads to menopausal syndrome characterized by vasomotor symptoms, atrophic vaginitis, osteoporosis and increased incidence of ischemic heart disease. Many of these symptoms can be prevented by starting HRT. The HRT is indicated in those women who are troubled by these symptoms. For vaginal atrophy a short course of oestrogen cream locally may be enough. Whereas for those with vasomotor symptoms require oral therapy for atleast 1 year or upto the age of 50 years. If the aim of HRT is to increase the bonemass and improve osteoporosis then the duration should be minimum of 10 years. HRT can be given with conjugated oestrogens or natural oestrogens. In those with intact uterus the drug must be given cyclically for 21 days, with an addition of progestogen for the last 10 days of the cycle. For those women who have undergone hysterectomy, the low dose oestrogens can be given alone continuously and there is no need for progestogens. The addition of progestogen may take away the benefit of low dose oestrogen in preventing ischemic heart disease.

- I: Hormone replacement therapy, for inducing secondary sexual characters in hypogonadism, for contraception.
- C/I: Pregnancy, oestrogen depended cancer, thrombophlebitis, thromboembolism, liver disease, breast feeding and undiagonised vaginal bleeding.
- P/C: Unopposed exposure to oestrogens pre dispose to cystic hyperplasia of the endometrium and endometrial cancer, migraine, fibro cystic disease of heart, thromboembolism and precipitate porphyria.

S/E: Nausea, vomiting, breast tenderness, weight gain, cholestatic jaundice, headache, depression.

P/A & Dose :

Conjugated oestrogen	Tablet	0.625 mg, 1.25 mg
	Injection	25 mg vial

Dose : 0.625 - 1.25 mg daily

Ethinyl oestradiol

Tablet	0.01 mg, 0.02 mg, 0.05 mg, 1 mg
Injection	10 mg/mL
Patch	25 mcg, 50 mcg, 100 mcg.

Combination preparation with other derivatives are also available.

Dose : Menopausal symptoms - 10 to 20 mcg daily.

Hormone deficiency - 10 to 50 mcg daily.

Contraception - 20 to 50 mcg daily depending on preparation.

Ethyl oestrenol

Tablet	2 mg
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Dose : 4 mg/day.

Oestradiol

Injection	10 mg
Gel	3 mg/5 g
Patch	0.025, 0.05, 0.1 mg (release/day)

Dose : Menopausal symptom - 1 to 2 mg/day for 3 weeks followed by 1 week off.

Breast cancer - 10 mg t.d.s for 3 months.

Osteoporosis - 0.5 mg/day for 3 weeks immediately following menopause.

Oestriol	Tablet	1 mg, 2 mg
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Dose : Oestrogen deficiency symptom due to menopause - 8 to 16 mg daily for 1 week followed by a maintenance dose of 2 to 4 mg/day.

D/I: Liver metabolism is enhanced by rifampicin, barbiturates and phenytoin. Effectiveness of anti coagulants decreased, toxic effect of imipramine may be enhanced.

Cost: Conjugated oestrogen

Tab	1.25 mg	(20)	Rs. 110.00 - 115.00
Inj	25 mg	(vial)	Rs. 65.00 - 70.00

Ethinyl oestradiol

Tab	0.01 mg	(10)	Rs. 9.00 - 12.00
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7. Drugs used in Endocrine Disorders

Inj	10 mg/mL	(1 mL)	Rs. 20.00 - 22.00
Patch	50 mcg	(2 nos.)	Rs. 110.00 - 115.00
Ethyl oestrenol			
Tab	2 mg	(10)	Rs. 19.00 - 20.00
Oestradiol			
Inj	10 mg	(1 mL)	Rs. 20.00 - 25.00
Gel	3 mg/5 g	(80 g)	Rs. 320.00 - 330.00
Oestriol			
Tab	2 mg	(30 mg)	Rs. 70.00 - 75.00

Tibolone

It is a synthetic preparation with oestrogen and progestogen activity with mild androgenic activity and is ideally suited for treating vasomotor symptoms of menopause and also for the prophylaxis of osteoporosis.

I: Menopausal syndrome

C/I: Hormone dependent tumors, history of thromboembolism, severe liver disease, pregnancy, history of cardio vascular or cerebro vascular disease, premenopausal women.

P/C: Renal impairment, epilepsy, migraine, diabetes mellitus and hypercholestrelemia.

S/E: Weight gain, ankle edema, abdominal pain, gastrointestinal disturbances, arthralgia, myalgia, rash, pruritis.

P/A: Tablet 2.5 mg

Dose: 2.5 mg o.d.

D/I: Sensitivity to anticoagulants increased, enzyme inducers like phenytoin, carbamazepine and rifampicin, accelerate, tibolone metabolism. Insulin or oral hypoglycemic requirement increased in diabetics

Cost: Tab 2.5 mg (28) Rs. 980.00

7.6.1.2 Progestogens

These are important female hormone concerned with reproduction. There are two group of progestogens available for clinical use.

1. Progesterones and its analogues : dihydrogestrone, hydroxy progesterone and medroxy progesterone.
2. Testosterone analogues : norethisterone, norgestron, digesterol, norgestimate, gestodens.

The testosterone derivatives are more androgenic than progesterone derivatives, but both do not cause virilization.

Progesterone

I: Progesterones are mainly use for the treatment of endometriosis, menorrhagia, severe dysmenorrhoea, premenstrual tension and for habitual abortions. Progesterones is also used as part of hormone replacement therapy in women with uterus and as a part of contraceptive medication.

C/I: Pregnancy, lactation, thromboembolism, hormone dependent carcinoma, incomplete abortion, liver diseases.

P/C: Use with caution in hypertension, mental depression, renal diseases, diabetes, asthma, epilepsy and migraine.

S/E: GI disturbances, acne, oedema, weight gain, changes in libido, altered menstrual cycle, virilization of female foetus, congenital abnormalities. Sterile abscess with i.m. injection, anal soreness and flatulence with rectal administration, thromboembolic disorders and possible foreign body carcinogenesis with intradermal implants.

P/A: Capsule 100 mg

Dose: Individualised dosing by physician.

D/I: Decreases effect of tricyclic antidepressants, hypoglycemic agents and anticoagulants.

Cost: Cap 100 mg (10 x 3) Rs. 680.00 - 690.00

Dydrogesterone, Medroxy ProgesteroneAcetate, Norethisterone*, Hydroxyprogesterone

I, C/I, P/C, S/E, D/I: Same as for progesterone.

P/A: Dydrogesterone

Tablet 5 mg

Medroxyprogesterone

Tablet 2.5 mg, 5 mg and 10 mg

Injection 150 mg

Norethisterone

Tablet 5 mg

Injection 200 mg

Hydroxyprogesterone

Injection 500 mg

Dose: Endometriosis: 10 mg t.d.s. for 90 days or 10 mg t.d.s. for 6 cycles.

Habitual abortion: 10 mg b.d. for days 11 - 25 cycle till conception.

D.U.B: 10 mg b.d. with oestrogen for 5 - 7 days to arrest bleeding and for 11- 25 th day of cycle to prevent bleeding.

Dysmenorrhoea: 10 mg b.d. from 5 th to 25 th day of cycle.

Premenstrual tension: 10 mg b.d. from 12 - 26 th day of cycle.

Cost: Dydrogesterone Tab 5 mg (10) Rs 112.00 - 113.00

Medroxyprogesterone

Tab	10 mg	(10)	Rs. 35.00 - 55.00
Inj	150 mg	(1mL)	Rs. 150.00 - 151.00

Norethisterone

Tab	5 mg	(10)	Rs. 30.00 - 35.00
Inj	200 mg	(1mL)	Rs. 127.00 - 128.00

Hydroxyprogesterone

Inj	500 mg	(2 mL)	Rs. 55.00 - 250.00
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7.6.2 Male sex hormones

Testosterone and its esters are the male sex hormones (androgens) available for clinical use. These produce masculinization in hypogonadal male and also has anabolic effects. When given to normal male it will suppress pituitary gonadotropins and suppress spermatogenesis and can result in testicular atrophy. Androgens given to hypopituitary males can produce normal secondary sexual characters and potency but for inducing spermatogenesis gonadotropins are required. When androgens are used in treating boys with delayed puberty, epiphyseal fusion and short stature may result.

Intramuscular preparations of testosterone esters - enanthate or propionate or mixtures are used for replacement therapy. They should be given once in 2 - 4 weeks, depending on the dose and clinical status. The oral preparations of testosterone undecanoate or mesterolone, which has to be taken daily in multiple doses to get adequate clinical response.

Testosterone and its esters ☆

- I: Primary and secondary hypogonadism, breast cancer, delayed puberty, impotence and male climacteric symptoms.
- C/I: Breast cancer in men, prostate cancer, hypercalcemia, pregnancy, nephrosis.
- P/C: Cardiac, renal and hepatic impairment, elderly, ischemic heart disease, hypertension, epilepsy, migraine.
- S/E: Headache, depression, sodium retention with oedema, hypercalcemia, prostate cancer, seborrhoea, acne, premature closure of epiphysis, suppression of spermatogenesis.
- P/A: Testosterone Capsule 40 mg
 Injection 25 mg, 50 mg, 100 mg and 250 mg
 Ointment 2 % w/w, 5 % w/w
 Patch 4 mg

Injections containing combination of esters of testosterone are also available.

Fluoxymesterone Tablet 2 mg, 5 mg, 10 mg

Methyl testosterone Tablet 10 mg, 25 mg
Capsules 10 mg

Dose: 25 - 50 mg i.m. every 1 - 2 weeks for 6 - 8 weeks.

Androgen deficiency : 120 - 160 mg/day for 2 - 3 weeks.

D/I: Potentiates anticoagulants, and oral hypoglycemic agents.
Rifampicine and phenobarbitone may increase the rate of metabolism of testosterone.

Cost: Testosterone Cap 40 mg (15) Rs. 90.00 - 93.00
Inj 250 mg(1 mL) Rs. 81.00 - 82.00

Other preparations and esters are not freely available.

Mesterolone

I:, C/I:, P/C:, S/E: Same as for testosterone

, P/A: Tablet 5 mg

Dose: 25 mg t.d.s. orally.

D/I: Reduce effect of anticoagulants and hypoglycemic agents. Liver enzyme inducing drugs increase metabolism of mesterolone.

Cost: Tab 25 mg (10) Rs. 107.00 - 115.00

7.6.3 Antiandrogens

These are drugs used to counter act the effect of circulating androgens. The clinical situations where these used are to control hypersexuality and prostate cancer in male and hirsutism and acne in females. The main drugs under this category are cyproteron acetate, finasteride and flutamide. Other drugs like spironolactone and ketoconazole are also having some antiandrogenic effect, but they do not come under this category. Cyproterone acetate is a testosterone receptor blocker while finasteride is a specific inhibitor of enzyme 5 alpha reductase which converts testosterone to active DHT. Flutamide is androgen receptor blocker.

Cyproteron Acetate

I: Male hypersexuality, prostatic cancer, acne and hirsutism in female.

C/I: Hepatic disease, severe diabetes mellitus, sickle cell anemia and depression.

P/C: Periodically assess blood counts and hepatic functions.

S/E: Fatigue lastitude, breathlessness, gynaecomastia, oligospermia.

P/A: Tablet 50 mg
Injection 100 mg

Dose: Oral 200 - 300 mg/day in divided doses after meal, reduced after orchiectomy to 100 to 200 mg/day.

Parenteral 300 mg/week, reduced after orchiectomy to 300 mg every 2 week.

D/I: When given to women along with ethinyl oestradiol the adverse

7. Drugs used in Endocrine Disorders

effects associated with oral contraceptives may occur.

Cost: Not freely available.

Finasteride

I: Benign prostate hyperplasia, acne and hirsutism in females.

C/I: Hypersensitivity, pregnancy, lactation and neonates.

P/C: Obstructive uropathy, prostate cancer.

S/E: Impotence, decreased libido and ejaculation, breast tenderness and enlargement, hypersensitivity reactions

P/A: Tablet 5 mg

Dose: 5 mg o.d.

D/I: Increases clearance of theophylline, half-life of aminophylline may be reduced.

Cost: Tab 5 mg (10) Rs. 85.00 - 86.00

Flutamide

I: Advanced prostate cancer. Used to cover the tumour 'flare' which may occur after commencing gonadorelin analogue administration.

C/I: Hypersensitivity, pregnancy.

P/C: Cardiac disease, monitor hepatic function.

S/E: Gynaecomastia, nausea, vomiting, diarrhoea, increased appetite, insomnia, tiredness.

P/A: Tablet 250mg

Dose: 250 mg t.d.s.

D/I: Increased prothrombin time in patients on long-term warfarin treatment.

Cost: Tab 250 mg (10) Rs. 100.00

7.6.4 Anabolic steroids

These are agents which were claimed to have protein anabolic property and were promoted as such. All these anabolic agents have some androgenic property. They cause less virilization compared to androgens in women. Present indication for anabolic steroids are the management of aplastic anaemia in children and osteoporosis.

Nandrolone

I: Aplastic anemia, senile osteoporosis.

C/I: Severe hepatic failure, prostatic cancer, male breast cancer, pregnancy.

P/C: Cardiac and renal impairment, hepatic dysfunction, diabetes, hypertension.

S/E: Acute sodium retention with edema, virilization, amenorrhoea, oligospermia.

P/A: Injection 25 mg, 50 mg and 100 mg

Dose: 25 - 50 mg i.m. once a week (intermittently)

D/I: Effect of corticosteroids potentiated, reduces efficacy of cyclophosphamide, enhances bleeding due to warfarin and phenindione.

Cost: Inj 25 mg (1 mL) Rs. 24.00 - 50.00

Stanozolol

I: Vascular manifestation of bahcet's disease, hereditary angioedema.

C/I: Pregnancy, breast feeding, IDDM, carcinoma of breast and prostate, hepatic and renal disease.

P/C: Cardiac and renal impairment, women should be observed for any signs of virilization, changes in menstrual periods, facial hair growth.

S/E: Acne, hirsutism, amenorrhoea, sodium retention, oedema, euphoria, depression, cholestatic jaundice.

P/A: Tablet 2 mg
Capsules 2 mg

Dose: Hereditary angioedema : 2.5 - 10 mg o.d., reduce upto 2.5 mg alternate days.

D/I: Increased sensitivity to anticoagulants, decreased effect of oral hypoglycaemics, altered action of anticonvulsants.

Cost: Tab 2 mg (10) Rs. 28.00 - 29.00.
Cap 2 mg (10) Rs. 14.00 - 15.00

CHAPTER 8 : ANALGESICS AND ANTIINFLAMMATORY AGENTS

8.1 ANALGESICS

8.1.1 Non-Opioid Analgesics

8.1.2 Opioid Analgesics

8.1.3 Drugs for Trigeminal Neuralgia

8.1.4 Drugs for Migraine

Pain is the commonest symptom that takes patients to doctors. Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. The general principle of management of pain is to remove the cause of pain. This is often difficult to achieve and symptom relief of pain by analgesic drug is required.

The non-opioid drugs, paracetamol and aspirin and other non-steroidal anti-inflammatory drugs (NSAID) are particularly suitable for pain in musculoskeletal conditions, whereas the opioid analgesics are more suitable for severe visceral pain. NSAIDs are particularly useful for the treatment of patients with chronic diseases accompanied by pain and inflammation and also useful to relieve post-operative and post-traumatic inflammation and pain.

Compound analgesic preparations containing non-opioid and opioid analgesics are commonly used, but the advantages have not been substantiated. Moreover, there is the possibility of opioid side effects and the risk of dependence.

8.1.1 Non-Opioid Analgesics

Aspirin (Acetylsalicylic Acid)

Acts mainly through the inhibition of prostaglandin synthesis.

- I: Mild to moderate pain, pyrexia, pain and inflammation in rheumatic diseases and other musculoskeletal disorders, including juvenile arthritis; prophylaxis of cerebrovascular disease and myocardial infarction.
- C/I: Breast feeding, gastro-intestinal ulceration, haemophilia and other haemorrhagic diseases, hypersensitivity to aspirin.
- P/C: Asthma, allergy to aspirin, upper gastrointestinal bleeding foci, impaired renal or hepatic function, dehydration, pregnancy, elderly. Owing to an association with Reye's syndrome aspirin containing preparations are sparingly given to children below 12 years unless specifically indicated.
- S/E: High incidence of gastro-intestinal irritation with slight or symptomatic blood loss, increased bleeding time, bronchospasm and skin reactions in hypersensitive patients. Prolonged use may aggravate an existing haemorrhagic tendency. Purpura and subconjunctival haemorrhage may occur. Other adverse effects

include myocarditis, chronic salicylate intoxication (salicylism) which is characterised by dizziness, tinnitus and deafness.

P/A: Tablets: 50mg, 60mg, 75mg, 80mg, 100mg, 150mg, 300mg, 325mg, 500mg, 650mg.

Soluble tablets 300mg

Enteric coated tablets 75mg, 80mg.

Dose: Mild to moderate pain: 300-900 mg every 4-6 h or when necessary up to a maximum of 4 g /day.

Rheumatic disease and other musculoskeletal disorders : 0.3-1 g every 4 h; maximum in acute conditions 8 g daily;

Children with juvenile arthritis, upto 80 mg/kg in 5-6 divided doses, increased in acute exacerbation to 130 mg/kg. Doses should be taken soon after food.

For the prophylaxis and management of thromboembolic strokes and myocardial infarction at a dose of 75-150 mg is given daily indefinitely.

D/I: Avoid concomitant administration of NSAIDs since they may aggravate the side effects, anticoagulants since they may increase the risk of bleeding, antiepileptics due to enhancement of effects of phenytoin and valproate and corticosteroids due to increased risk of gastro-intestinal bleeding and ulceration

Cost :	Tab	75 mg	(14)	Rs. 8.00
	Soluble tab	325 mg	(10)	Rs. 2.00 - 3.00
	Enteric coated tab	75mg	(14)	Rs. 8.00 - 10.00

Paracetamol (Acetaminophen) ☆

I: Mild to moderate pain, pyrexia

C/I: Hypersensitivity

P/C: Hepatic and renal impairment, alcohol dependence

S/E: Rashes, blood dyscrasias, acute pancreatitis and hepatic failure after prolonged use . Doses above 4 g o.d. may be associated with hepatotoxicity and in large doses paracetamol is a lethal hepatotoxin and renal damage may occur following overdose.

Fatal dose is 12 to 25 g.

P/A: Tablets: 300 mg, 500 mg, 650 mg.

Kid-Tab 250 mg.

Dispersible-tablets 125 mg.

Suspension 125mg/5mL.

Liquid 150mg/mL.

Drops 150mg/mL.

Injection 150mg/mL and 300mg/mL.

8. Analgesics and Antiinflammatory Agents

Dose: Oral, 0.5 - 1 g every 4-6 h to a maximum of 4 g o.d.,
Children upto 2 months 60 mg for post immunisation pyrexia;
Otherwise under 3 months 10 mg/kg (5mg/kg if jaundiced);
3 months to 1 year 60-120 mg,
1-5 years 120-250 mg
6-12 years 250-500 mg.
These doses may be repeated every 4-6 h when necessary up to a maximum of 4 doses in 24 h.
Injection 150-300 mg i.m.

D/I: Absorption of the drug is reduced by pethidine and propantheline.

Cost :	Tab 500 mg	(10)	Rs. 5.00
	Syrup 125 mg/5 mL	(60 mL)	Rs. 10.00
	Inj 150mg/mL	(2mL)	Rs. 4.00

Nefopam Hydrochloride

I: Moderate pain

C/I: Convulsive disorders, myocardial infarction, children.

P/C: Hepatic and renal dysfunction, urinary retention.

S/E: Nausea, nervousness, urinary retention, dry mouth, light headedness; less frequently vomiting, blurred vision, drowsiness, sweating, insomnia, tachycardia, headache, confusion and hallucinations, pink discoloration of urine.

P/A: Tablet 30 mg

Injection 20 mg/mL.

Dose: Oral, initially 60 mg t.d.s., adjusted according to response. The usual range is 30-60 mg t.d.s.

For persons above 65 years this dose is halved.

Parenteral dose i.m. injection, 20 mg every 6 h.

For children this drug is not recommended.

D/I: MAO inhibitors may alter the efficacy of nefopam. Concurrent use of tricyclic antidepressants may result in exaggerated antimuscarinic effects such as blurred vision, dry mouth, urinary retention and others.

Cost :	Tab 30 mg	(10)	Rs. 17.00
	Inj 20 mg	(1 mL)	Rs. 6.00

NSAIDs

8.1.2 Opioid Analgesics

Opioids act by interfering with the opioid receptors within the central nervous system and in peripheral tissues. Opioid analgesics are used to relieve

moderate to severe pain, particularly of visceral origin. Repeated administration may cause dependence and tolerance, but this is not a deterrent for the use of these drugs for the control of pain in terminal illness.

Opioid analgesics include morphine, pethidine, codeine, buprenorphine, dextropropoxyphené, pentazocine and tramadol.

Morphine ☆

- I: Moderate to severe pain particularly of visceral origin. This is the opioid of choice for the oral treatment of severe pain in palliative care, especially in cancer, peri-operative analgesia and enhancement of anaesthesia. It is indicated in myocardial infarction and acute pulmonary oedema.
- C/I: Avoid in acute respiratory depression, acute alcoholism and conditions where there is risk of paralytic ileus, pheochromocytoma and Addison's Disease. This is not indicated for acute abdominal pain. This has to be avoided in raised intracranial pressure, or head injury since in addition to interfering with respiration, they affect pupillary responses vital for neurological assessment.
- P/C: Hypotension, hypothyroidism, asthma, decreased respiratory reserve, prostatic hypertrophy, pregnancy and breast feeding, hepatic impairment; renal impairment and opioid dependence. Severe withdrawal symptoms occur if withdrawn abruptly.
- S/E: Nausea and vomiting, constipation, drowsiness, respiratory depression, hypotension, difficulty in micturition, ureteric and biliary spasm, dry mouth, sweating, headache, facial flushing, vertigo, bradycardia, palpitation, postural hypotension, hypothermia, hallucinations, miosis, decreased libido, rashes, pruritus and dependence.
- P/A: Tablets: 10 mg, 30 mg, 60 mg and 100 mg.
Injection: 15 mg/mL
10 mg/mL large vials of 100 mL.
- Dose: For acute pain morphine is given by s.c. or by i.m. injection, 10 mg every 4 h if necessary
Children upto 1 month 150 mcg/kg
1-12 months 200 mcg/kg
1-5 years 2.5-5 mg
6-12 years 5-10 mg.
- Peri-operative analgesia: by s.c. or i.m. injection, up to 10 mg 1-11/2 h before operation.
- Post-operative pain : by s.c. or i.m. 10 mg every 2-4 h if necessary.
- Morphine hydrochloride can be given by slow i.v. injection at a dose of 25-50% of the i.m. dose.
- Acute myocardial infarction : slow i.v., at the rate of 2mg/minute, to a total of 10 mg followed by a further 5-10 mg if necessary.

8. Analgesics and Antiinflammatory Agents

Elderly and frail patients, haemodynamic impairment - half the dose.

Acute pulmonary oedema, morphine is given by slow i.v. injection at the rate of 2mg/minute to a total of 5-10 mg.

Chronic pain, morphine sulphate is given orally or parenterally (s.c. or i.m.) in a dose of 5-20 mg regularly every 4 h. The dose may be increased in individual cases depending on the response to morphine. Oral dose is approximately double the corresponding i.m. dose and is to be given t.d.s or q.d.s.

Antidote

Naloxone can be used to reverse the respiratory depression. It is given by i.v. injection in a dose of 100-200 mcg (1.5-3 mcg/kg) per minute. If the response is inadequate, the dose is increased by 100 mcg every 2 min till the pupils become normal. Further dosage is by i.m. injection after 1-2 h.

Children - initially by i.v. in a dose of 10 mcg/kg. Subsequent doses 100 mcg/kg if there is no response to the standard dose.

D/I: Reduces the plasma levels of ciprofloxacin Dextropropoxyphene may enhance effect of carbamazepine. Enhance sedative and hypotensive effect with antipsychotics. Hyperpyrexia and CNS toxicity may occur with selegiline. The effects of metoclopramide and domperidone, are antagonised.

Cimetidine inhibits metabolism of opioid analgesics notably pethidine and there by leads to increased plasma concentration.

Note: Opioid drugs comes under schedule - H of Drugs and Cosmetics Act.

Cost:	Tab	10mg	(10)	Rs 7.00
	Inj	15mg	(1mL)	Rs 6.00

Prescriptions ordering such drugs should not be dispensed more than once. At the time of dispensing a prescription the pharmacist should note name, address of the doctor and the date of dispensing. No substitution of the drug should be made during dispensing. The pharmacist should file a copy of the prescription containing Schedule - H drugs. Drugs under Schedule - H should be stored under lock and key in either a drawer or a cupboard to which the customers have no access.

Buprenorphine hydrochloride

I: Moderate to severe pain, perioperative analgesia

C/I:, S/E:, P/C:, D/I: Similar to morphine.

P/A: Tablet 200 mcg,

Injection 300 mcg/mL and 300 mcg /2mL.

Dose: Sublingual - start with 200-400 mcg every 8 h, increasing if necessary to 200-400 mcg every 6-8 h.

Children over 6 months,	16 - 25 kg,	100 mcg;
	25 - 37.5 kg	100-200 mcg,
	37.5 - 50 kg	200-300 mcg.

Parenteral - i.m. or slow i.v. 300-600 mcg every 6-8 h;

Children over 6 months 3-6 mcg/kg every 6-8 h up to a maximum of 9mcg/kg.

Cost: Tab 200 mcg (10) Rs. 18.00

Inj 0.3 mg (1 mL) Rs. 10.00

Codeine Phosphate ☆

I: Moderate to severe pain.

Symptomatic relief of diarrhoea.

Irritant non-productive cough.

C/I;S/E;P/C;D/I: Same as morphine salts but milder. Use of cough suppressants containing codeine or similar opioid analgesics is not generally recommended in children and should be avoided altogether in those under 1 year of age.

P/A: Tablet 10 mg

Linctus 15 mg/5 mL.

Dose: Pain relief:

Oral: 30-60 mg every 4 h, to a maximum of 240 mg daily;

Children 1-12 years 3 mg/kg o.d. in divided doses.

Diarrhoea 30 mg given oral t.d.s. – q.d.s. daily in adults.

Codeine is not recommended in children.

Cost :	Tab 10mg	(10)	Rs 6.00
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Linctus	(100 mL)	Rs. 30.00
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Dextropropoxyphene Hydrochloride

I: Moderate to severe pain

C/I:,P/C:,S/E:, D/I: Same as for morphine salts. Additional side effects include occasional hepatotoxicity and porphyria. Over dosage leads to convulsions. Contra-indicated in those who have suicidal tendency or tendency for addiction.

P/A: Capsule 65 mg

Dose: 65 mg every 6-8 h when necessary. Not recommended for children.

Cost: Cap 65 mg (10) Rs. 9.00

Fentanyl Citrate

I: Chronic intractable pain due to cancer.

Analgesia during operation and enhancement of anaesthesia.

8. Analgesics and Antiinflammatory Agents

As a respiratory depressant in assisted respiration.

C/I: P/C: S/E: D/I: Same as for morphine salts. Local reaction at the site of injection such as rash, erythema and itching.

P/A: Injection 50mcg/mL

Dose: Premedication : i.m. injection in a dose of 50-100 mcg 30-60 min prior to surgery.

Adjunct to general anaesthesia : low doses in minor but painful procedures, given i.v. 2 mcg/kg repeated if necessary.

Major surgery : moderate doses of 2-20 mcg/kg are given initially. When there are signs of lightening of anaesthesia 25-100 mcg are given i.v. or i.m. This additional dose is not based on bodyweight.

High doses are required in open heart surgery or similar complex procedures. Initial dose is 25-50 mcg/kg i.v. Additional doses of 25 mcg or more are indicated if there is lightening of anaesthesia irrespective of the patient's body weight.

As an adjunct to regional anaesthesia: 50-100 mcg by i.m. or slow i.v. injection given in 1-2 min.

Post-operative pain : 50-100 mcg i.m. .

Children: 2-12 years : 2-3 mcg/kg for induction and maintenance.

Cost : Inj 50 mcg/mL (5 x 2 mL) Rs. 175.00

Pentazocine Hydrochloride ☆

I: Moderate to severe pain.

C/I: S/E: P/C : D/I: Similar to morphine salts; occasional hallucinations.

It has both agonist and antagonist opiod properties and precipitates withdrawal symptoms including pain in patients who are dependent on other opioids. This drug has to be avoided in patients dependent on opioids and in those with systemic or pulmonary hypertension, heart failure, and porphyria. It should be avoided after myocardial infarction since it may increase the cardiac work.

P/A: Tablet 25 mg

Injection 30mg/mL

Dose: Oral :50 mg every 3-4 h preferably after food (range 25-100 mg);

Children 6-12 years 25 mg.

Parenteral : by s.c., i.m. or i.v.

Moderate pain, 30 mg

Severe pain 45-60 mg every 3-4 h when necessary.

Children over 1 year by s.c. or i.m. up to 1mg/kg, by i.v. up to 500mcg/kg.

If repeated injections are required the drug should be given by i.m. but same injection site should not be repeated.

Cost : Inj 30 mg/mL (1 mL) Rs. 5.00 – 17.00

Pethidine Hydrochloride ☆

I: Moderate to severe pain, obstetric analgesia, peri-operative analgesia and premedication.

C/I:, P/C:, S/E:, D/I: Similar to morphine salts.

P/A: Tablet 50 mg, (not freely available)

Injection 50mg/mL,

Dose: Pain relief : Oral 50-150 mg every 4 h; child 0.5-2mg/kg.

Parenteral s.c., i.m. 25-100 mg repeated after 4 h; slow i.v. injection 25-50 mg, repeated after 4 h.

Children i.m. 0.5-2mg/kg.

Obstetric analgesia : s.c. or i.m., 50-100 mg, repeated after 1-3 h if necessary; maximum 400 mg in 24 h.

Premedication : i.m. 25-100 mg 1 h before operation.

Children 0.5-2 mg/kg

Adjunct to nitrous oxide-oxygen anaesthesia : given by slow i.v. injection, 10-25 mg, repeated when required.

Postoperative pain- s.c. or i.m., 25-100 mg, every 2-3 h if necessary, Children, i.m., 0.5-2 mg/kg.

Note: Pethidine has to be used with caution since dependence on this drug develops very frequently.

Cost : Inj 50mg (2mL) Rs 8.00

Tramadol Hydrochloride

I: Moderate to severe pain

C/I:, P/C:, S/E:, D/I: Similar to morphine salts. It may cause hypotension, or occasionally hypertension; anaphylaxis, hallucinations, confusion, seizures in those with epileptic tendency (convulsion is precipitated especially by rapid i.v. injection). To be avoided in pregnancy and breast-feeding. For children this drug is not recommended. Not a suitable substitute in opioid dependent patients during weaning.

P/A: Tablets and capsules 50 mg

Injection 50mg/mL

Dose: Oral: 50-100 mg every 4h or larger

The total dose to be limited to 400mg or less in 24h.

Parenteral dosage:

i.m. or i.v. (over 2-3 min) or by i.v. infusion, 50-100 mg every 4-6 h.

Post operative pain, 100 mg initially, then 50 mg every 10-20 min.

Maximum of total dose during the first hour should not exceed 250 mg including the initial dose. Thereafter 50-100 mg is given every 4-6 h upto a maximum of 600 mg daily.

Cost : Cap 50 mg (10) Rs. 60.00

Inj 50 mg/mL (2 mL) Rs. 25.00

8. Analgesics and Antiinflammatory Agents

8.1.3 Drugs for Trigeminal Neuralgia

Carbamazepine ☆

It is primarily an anticonvulsant. When used during the acute stages of trigeminal neuralgia it reduces the frequency and severity of attacks. It has no effect on other forms of headache. A dose of 100 mg once or twice a day given initially and the dose slowly increased until the best response is obtained. Most patients require 200 mg t.d.s. or q.d.s. A few may require an increased total daily dosage of upto 1.6 g. Plasma carbamazepine concentration should be preferably monitored when high doses are given. Occasionally extreme dizziness may occurs. This is an indication for lowering the dose and gradual readjustment.

Some cases of trigeminal neuralgia respond to phenytoin given alone or in conjunction with carbamazepine. A combination of phenytoin and carbamazepine is required only in refractory cases or in those unable to tolerate high doses of carbamazepine. It is also useful in glossopharyngeal neuralgia.

Note : Although tricyclic antidepressants are not indicated for true trigeminal neuralgia they are more effective than carbamazepine in post-herpetic neuralgia and may also be useful in oral and facial pain, particularly if associated with depression.

Cost : Tab 200 mg (10) Rs. 20.00

8.1.4 Drugs for MIGRAINE

Treatment of acute attack of migraine

Acute attacks of migraine may be relieved by common analgesics or specific drugs such as ergotamine and the 5HT₁ agonist like sumatriptan. An anti-emetic may also be given if nausea and vomiting are prominent. Many cases of migraine respond to analgesics such as aspirin or paracetamol, but since peristalsis is often reduced during migraine attacks oral medication may not be sufficiently well absorbed. Dispersible or effervescent preparations are preferable for better absorption. It is extremely important to instruct the patients to take analgesics as soon as they get premonitory symptoms like fortification spectra or scintillating scotomas or any other subjective feelings.

Anti-emetics such as metoclopramide orally or by i.m. injection or other antiemetics such as phenothiazine and antihistamines relieve the troublesome nausea. Metoclopramide has the added advantage of promoting gastric emptying and normal peristalsis.

Ergotamine tartrate

I: Acute attacks of migraine and migraine variants unresponsive to analgesics.

C/I: Peripheral vascular disease, coronary heart disease, obliterative vascular disease, Raynaud's syndrome, hepatic and renal

impairment, sepsis, severe or inadequately controlled hypertension, hyperthyroidism, pregnancy and breast feeding, porphyria.

P/C: Risk of peripheral vasospasm, elderly patients. Not effective for migraine prophylaxis.

S/E: Nausea, vomiting, vertigo, abdominal pain, diarrhoea, muscle cramps and occasionally increased headache, precordial pain, myocardial ischaemia, rarely myocardial infarction.

Repeated high doses may cause ergotism with gangrene, confusion, pleural and peritoneal fibrosis.

P/A : Only combinations of ergotamine 1 – 2 mg along with other analgesic and antihistamines are available.

Dose: 2 tabs orally every 30 min (1-2 mg) until complete relief is obtained. Not more than 6 mg o.d.

Children 3-9 years: one fourth of adult dose.

10-14 years half of adult dose.

D/I: Ergotism is precipitated by erythromycin and possibly by azithromycin with beta blockers and 5HT₁ agonist increase the peripheral vasoconstriction.

Dihydroergotamine ☆

I, C/I, P/C, S/E, D/I : Same as for ergotamine tartrate

P/A: Tablet 1 mg

Injection 1mg/mL

Dose: Sublingually 2 mg until relief is obtained, should not exceed maximum dose 6mg/day.

s.c., i.m. and i.v. doses of 1 mg every hour to a maximum of 3mg daily.

If rapid effect is desired 2 mg may be given i.v and 1 mg i.v is repeated in 30 - 60 min to a total of 3 mg o.d..

Cost : Tab 1mg (10) Rs. 34.00

Inj 1 mg (1 mL) Rs. 5.00

Sumatriptan

It is a selective 5-HT₁ like receptor agonist and it acts by constriction of dilated intracranial vessels.

I: Acute treatment of migraine attacks not responding to other drugs, complicated migraine; cluster headaches.

C/I: Ischaemic heart disease, previous myocardial infarction, coronary vasospasm including Prinzmetal's angina; uncontrolled hypertension. Should not be used for prophylaxis.

P/C: Should be used with caution in conditions which predisposes to coronary artery disease, hepatic impairment, pregnancy and breast

8. Analgesics and Antiinflammatory Agents

feeding. Sumatriptan is recommended as monotherapy and should not be taken concurrently with other anti migraine drugs.

In the presence of ischaemic heart disease, sumatriptan should not be given i.v., since it may precipitate angina.

S/E: Sensations of tingling, heat, heaviness, pressure or tightness of any part of the body; flushing; dizziness, feeling of weakness, fatigue; nausea and vomiting, transient increase in blood pressure, hypotension, brady or tachycardia and seizures.

P/A: Tablets 25 mg, 50 mg and 100 mg.

Injection ampoule 6mg/0.5mL (5mL)

Dose: Oral 50 - 100 mg, as soon as possible after the onset of migraine. Unresponsive patients should not take a second dose for the same attack. The dose can be repeated if migraine recurs upto a maximum of 300 mg in 24 h.

Parenteral - given s.c. using auto-injector in a dose of 6 mg as soon as possible after the onset. The dose should not be repeated during the same attack but it can be repeated one hour later if migraine recurs, upto a maximum of 12 mg in 24 h.

Cost : Tab 50 mg (1) Rs. 36.00 – 55.00

Inj 6mg/0.5 mL (5mL) Rs. 10.00

Beta blockers like propranalol, tricyclic antidepressants like amitryptiline, sodium valporate, calcium channel blockers (verapamil and nifedipine) and cyproheptadine and flunarizine are useful drugs in the prophylaxis of migraine.

Prophylaxis of Migraine

In patients with more than one attack a month, either of the two main prophylactic agents may be tried i.e. beta-blockers and tricyclic antidepressants

Beta blockers

(Propranalol, metoprolol, nadolol and timolol)

Most commonly used propranalol :Oral : 40 mg b.d. or t.d.s.

It may also be given as a single daily dose of a long acting preparation.

Tricyclic antidepressants

Amitryptiline :Start with 10 mg h.s. increasing to a maintenance dose of 50 – 75 mg h.s. in some cases up to 100 mg may be necessary.

Calcium channel blockers

Verapamil and nifedipine : 5 mg b.d or t.d.s.

Sodium valporate : 300 mg b.d.

Cyproheptadine :In children and in young adults start with 2 mg single dose to be increased to 4 mg if necessary. Adult start with 4 mg maintenance and 4 mg every 4 – 6 h.

Flunarizine

This drug has histamine H₁ receptor blocking action and calcium channel blocking effect.

I: Prevention of migraine.

C/I: Pregnancy, lactation, acute porphyria, gastro-intestinal and urinary tract obstruction.

S/E: Sedation, dry mouth extrapyramidal symptoms.

P/A: Tablet 5 mg, 10 mg.

Dose: 5-10 mg o.d. in the evening.

D/I: Plasma levels reduced by phenytoin, carbamazepine and valproic acid

Cost: Tab 5 mg (10) Rs. 10.00

8.2 DRUGS USED IN THE TREATMENT OF MUSCULOSKELETAL AND JOINT DISORDERS

These are mainly used in the treatment of rheumatoid diseases and other conditions when the inflammatory processes are to be controlled.

8.2.1 Non-steroidal anti-inflammatory drugs

8.2.2 Corticosteroids

8.2.3 Drugs which suppress the rheumatic disease process

8.2.4 Drugs for treatment of gout

8.2.5 Nonspecific analgesic agents

8.2.6 Drugs for the relief of soft tissue inflammation

8.2.1 Non-steroidal anti-inflammatory drugs (NSAIDs)

The non-steroidal anti-inflammatory drugs (NSAIDs) have diverse properties despite common therapeutic actions and adverse effects. NSAIDs have both lasting analgesic and anti-inflammatory effects, which make them particularly useful for the treatment of continuous or regular pain, associated with inflammation. As analgesic agents they are different from narcotic analgesics on several counts:

1. They are effective only in superficial pain of somatic origin, but not in deep visceral pain
2. Effective in pain of low to moderate intensity
3. In ordinary doses they do not cause respiratory depression
4. Abuse potential is similar to that of paracetamol, but paracetamol is preferred, particularly in the elderly

Differences in anti-inflammatory activity between different NSAIDs are small, but there is considerable variation in individual patient response. The analgesic effect should normally be obtained within a week, whereas the

8. Analgesics and Antiinflammatory Agents

anti-inflammatory effect may not be achieved for upto three weeks. NSAIDs differ in the incidence and type of side effects.

NSAIDs act by inhibiting the biosynthesis and release of prostaglandin but they do not alter the synthesis of other inflammatory mediators.

CLASSIFICATION OF NSAIDs

1. Salicylic acid derivatives	Aspirin
2. Para-aminophenol derivatives	Paracetamol
3. Arylpropionic acids	Ibuprofen, naproxen, ketoprofen
4. Heteroaryl acetic acids	Diclofenac
5. Indole and indene acetic acids	Indomethacin
6. Anthranilic acids	Mefenamic acid
7. Enolic acids	Piroxicam, tenoxicam
8. Sulfonanilide	Nimesulide
9. Alkanones	Nabumetone

CAUTIONS AND CONTRAINDICATIONS:

NSAIDs should not be given to patients with active peptic ulceration. Gastro-intestinal bleeding and ulceration may be precipitated by them. Omeperazole and H_2 receptor antagonists may be used to prevent and treat NSAIDs - associated peptic ulcers.

Should be used with caution in the elderly. Contra-indicated in allergic disorders, in patients with a history of hypersensitivity to aspirin or any of the NSAIDs, during pregnancy and breast feeding, and in coagulation defects.

For patients with renal, cardiac, or hepatic impairment, NSAIDs have to be given with caution.

Most of the NSAIDs are available in gel form for local application over inflamed joints and other tissues. It is claimed that transdermal absorption of the active ingredients occur and that the active drug reaches the site of lesions. In many cases symptomatic relief may occur.

SIDE-EFFECTS

Gastro-intestinal discomfort, nausea, diarrhoea, and occasionally bleeding and ulceration. Dyspepsia may be minimised by taking these drugs with food or milk. Other side effects include hypersensitivity reactions such as rashes, angioedema and bronchospasm; headache, dizziness, vertigo, hearing disturbances such as tinnitus, photosensitivity, haematuria and blood dyscrasias. Fluid retention may occur and precipitate congestive heart failure in elderly patients. May provoke renal failure especially in patients with pre-existing renal impairment. Hepatic damage, Stevens-Johnson syndrome and toxic epidermal necrolysis are other rare side effects.

DRUG INTERACTIONS

With ACE inhibitors the hypotensive effect is reduced. There is increased risk of renal damage and hyperkalaemia.

Concomitant administration of two or more NSAIDs including aspirin increase the adverse side-effects.

Anticoagulant effects of warfarin and other drugs are enhanced.

Effect of sulphonylureas is enhanced.

Effect of phenytoin is enhanced.

The hypotensive effect of beta-blockers is reduced. There is increased risk of gastro-intestinal bleeding with corticosteroids. The risk of nephrotoxicity of NSAIDs is increased by diuretics NSAIDs reduce excretion of baclofen and aggravate the toxicity of the latter .

Aspirin (see section 8.1.1.)

Paracetamol (see section 8.1.1.)

Ibuprofen ☆

I: Pain and inflammation in rheumatic disorders including juvenile arthritis and other musculo skeletal disorders. Mild to moderate pain including dysmenorrhoea; postoperative analgesia, fever and pain in children.

C/I:, P/C:, S/E:, D/I: Common for all NSAIDs.

P/A:	Tablets	200 mg, 400 mg, 600 mg.
	SR-Capsules	300 mg, 600mg.
	Syrup	125 mg / 5mL.
	Gel	10 % w/w

Dose: Initially 1.2 - 1.8 g o.d. in 3-4 divided doses preferably after food; increased if necessary to a maximum of 2.4 g o.d.; maintenance dose of 0.6-1.2 g o.d. may be adequate.

Children 20mg/kg o.d. in divided doses. Juvenile arthritis, upto 40 mg/kg o.d.

Cost :	Tab 200 mg	(10)	Rs. 5.00
	Cap 300 mg	(10)	Rs. 10.00
	Gel 10 % w/w	(30 g)	Rs. 33.00

Naproxen

I: Pain and inflammation in rheumatic diseases including juvenile arthritis and other musculoskeletal disorders, mild to moderate pain including dysmenorrhoea, acute gout.

8. Analgesics and Antiinflammatory Agents

C/I:,P/C:,S/E:,D/I: Same as for NSAIDs .

P/A: Tablets 250 mg, 275mg, and 500 mg.

Gel 10 % w/w

Dose: 0.5-1g daily in 2 divided doses or 1 g o.d.

Acute musculoskeletal disorders and dysmenorrhoea: 500mg initially, then 250 mg every 6-8 h as required; upto a maximum dose of 1.25 g/day.

Acute gout: 750 mg initially, then 250 mg every 8 h until the attack subsides.

In general for children under 16 years this drug is not recommended. However, for children over 5 years, with juvenile arthritis, 10 mg/kg o.d. in 2 divided doses may be given.

Cost : Tab 250 mg (10) Rs. 28.00 – 31.00

Gel 10 % w/w (20g) Rs. 25.00 – 28.00

Ketoprofen

I: Rheumatic diseases, other acute musculoskeletal disorders, acute gout, dysmenorrhoea and after orthopaedic surgery.

C/I: P/C:, S/E:, D/I: Same as for NSAIDs. Local pain at the site of injection site may be pronounced. Not recommended for children.

P/A: Tablets 50 mg, 100 mg,

Capsules 50 mg, 100 mg,

Injection 50mg/mL.

Dose: Oral: for rheumatic diseases, 100-200 mg o.d. in 2-4 divided doses with food.

Pain, dysmenorrhoea, 50 mg up to t.d.s.

Parenteral : by deep i.m. injection into gluteal muscle, 50-100 mg every 4 h upto a maximum of 200 mg in 24 h for upto 3 days.

Cost : Tab 50 mg (10) Rs. 7.00 – 12.00

Caps 50 mg (10) Rs. 11.00

Inj 50 mg/mL (2 mL) Rs. 24.00 – 25.00

Gel 2.5% (20 g) Rs. 30.00

Diclofenac Sodium ☆

I: Rheumatic diseases including juvenile arthritis and other musculoskeletal disorders, acute gout, postoperative pain.

C/I:, P/C:, S/E:,D/I: Common for all NSAIDs. Avoid in porphyria.

P/A: Tablets 50 mg and 100mg,

SR-Tablets 75mg, 100mg,

CR-Caps 100 mg,

Dispersible-Tablet 50 mg,

Injection 25mg/mL.

Gel 1% w/w.

Dose: Oral - 75 to 150 mg o.d. in 2-3 divided doses after food.

Parenteral - deep i.m. injection into gluteal muscle, 75 mg o.d. or b.d. for upto 2 days.

Ureteric colic - 75 mg, initially and the same dose to be repeated after 30 minutes if necessary.

Cost :	Tab 50 mg	(10)	Rs. 4.00 – 8.00
	Inj 25 mg/mL	(3 mL)	Rs. 4.00 – 6.00
	Gel 1 % w/w	(30 g)	Rs. 20.00 - 23.00

Indomethacin

I: Rheumatic disease and other acute musculoskeletal disorders, acute gout, dysmenorrhoea.

C/I: This drug is not recommended for children.

P/C:, D/I: Similar to other NSAIDs. Administer with caution in epilepsy, parkinsonism and psychiatric disturbances.

S/E: In addition to the usual adverse side effects of NSAIDs, blood dyscrasias especially thrombocytopenia, hypertension, hyperglycaemia and peripheral neuropathy.

P/A:	Tablets	25 mg
	Capsules	25 mg and 50 mg
	SR-Tablet	75 mg
	SR-Capsules	75 mg
	TR-Capsules	75 mg
	Eye drops	1 % w/w

Dose: Oral dosage in rheumatic diseases, 50-200 mg o.d. in divided doses, with food.

Acute gout, 150-200 mg o.d. in divided doses

Dysmenorrhoea up to 75 mg o.d.

Cost :	Tab 25 mg	(10)	Rs. 6.00 – 10.00
	Cap 25 mg	(10)	Rs. 5.00 – 12.00
	SR-Tab 75 mg	(10)	Rs. 25.00 – 30.00
	SR-Cap 75 mg	(10)	Rs. 30.00 – 32.00
	TR-Cap 75 mg	(10)	Rs. 18.00 – 20.00
	Eye drops 1% w/w	(5 mL)	Rs. 23.00 – 26.00

Meferamic Acid

I: Pain and inflammation in rheumatic diseases including juvenile

8. Analgesics and Antiinflammatory Agents

arthritis, other musculoskeletal disorders, mild to moderate pain including dysmenorrhoea.

C/I:,P/C:,S/E:,D/I: Same as for NSAIDs. Contra-indicated in inflammatory bowel disease.

Blood counts should be done regularly if the drug is given for long term treatment. It should be avoided in porphyria

P/A: Tablets 100mg, 250mg, 500 mg.

Capsules 250 mg, 500 mg.

Suspension 50mg/5mL.

Dose: 500 mg t.d.s. preferably after food ;

Children over six months, 25 mg/kg o.d. in divided doses for not more than 7 days, except in juvenile arthritis .

Cost :	Tab 500 mg	(10)	Rs. 15.00 –17.00
	Cap 500 mg	(10)	Rs. 20.00 – 25.00
	Susp 50 mg/5mL	(60 mL)	Rs. 7.00 – 14.00

Piroxicam

I: Pain and inflammation in rheumatic diseases including juvenile arthritis and other musculoskeletal disorders, mild to moderate pain including dysmenorrhoea, acute gout.

C/I:,P/C:,S/E:,D/I: Same as for NSAIDs. Not recommended for children except in juvenile arthritis.

P/A: Tablets 10mg and 20 mg,

Capsules 10mg and 20 mg,

Dispersible-tablet 20mg,

Injection 20mg/mL.

Gel 0.5 % w/w.

Dose: Oral: rheumatic diseases: initially 20 mg o.d., and maintenance dose 10-30 mg o.d., in single or divided doses.

Children over 6 years with juvenile arthritis and body weight less than 15 kg- 5 mg o.d.;

16-25 kg, 10 mg;

26-45 kg, 15 mg;

over 46 kg, 20 mg.

Acute musculoskeletal disorders, 40 mg o.d., in single or divided doses for 2 days, thereafter 20 mg o.d. for 7-14 days.

Acute gout, 40 mg initially followed by 40 mg o.d. in single or divided doses for 4-6 days.

Parenterally by deep i.m. injection into gluteal muscle, for the initial treatment of acute conditions, in a dose of 20 mg for short periods only. Injections also are not recommended for children

Cost :	Caps 20 mg	(10)	Rs.25.00
	Tab 20 mg	(10)	Rs. 30.00
	Inj 20 mg/mL	(2 mL)	Rs. 15.00
	Gel 0.5 %w/w	(30 g)	Rs. 20.00 - 45.00

Tenoxicam

I : Pain and inflammation in rheumatic disease and other musculoskeletal disorders.

C/I:,P/C:,S/E:,D/I: Same as of NSAIDs. For children this drug is not recommended.

P/A : Tablet 20 mg.

Dose : Rheumatic disease - 20 mg o.d.

Acute musculoskeletal disorders 20 mg o.d. for 7 days upto a maximum of 14 days.

Cost : Tab 20 mg (10) Rs. 55.00

Nimesulide

It belongs to the sulfonamide class of drug.

I : Rheumatic conditions, painful inflammatory conditions associated with musculoskeletal system, dysmenorrhoea and thrombophlebitis, post operative and dental pain, ENT inflammations.

C/I:, P/C:, S/E:, D/I: Being a selective inhibitor of inflammatory prostaglandin synthase (cox-2 selective inhibitor). Nimesulide claims to be free from the usual side effects common to other class of NSAIDs, Contraindicated in active peptic ulcer disease and hepatic impairment.

P/A : Tab 100 mg

Susp. 50 mg/mL

Gel 1% w/w

Dose : Pain and inflammatory conditions - Adult: 100 mg b.d

Children: 5 mg/kg/day in 2-3 divided doses .

Acute musculoskeletal and rheumatic conditions :

1 % Gel to be applied to affected site t.d.s. or q.d.s.

Cost : Tab 100 mg (10) Rs. 10.00 – 30.00

Susp. 50 mg/mL (60 mL) Rs. 13.00 – 17.00

Gel 1 % w/w (20 mg) Rs. 27.00 – 30.00

8.2.2CORTICOSTEROIDS

These are indicated as the primary drugs in specific conditions where there is a strong immunological disturbance as in rheumatoid arthritis and systemic lupus erythematosus, and as adjunct drugs in other painful

8. Analgesics and Antiinflammatory Agents

lesions where NSAIDs and analgesics are not fully successful. Prednisolone is given in doses of 7.5 mg o.d. but in severe cases a high initial dose of prednisolone (1-2mg/kg/bw) is given to induce remission and the dose is gradually reduced to the lowest maintenance dose.

Most of the cases of polymyalgia rheumatica and giant cell (temporal) arteritis respond only to corticosteroids. The usual initial dose of prednisolone in polymyalgia rheumatica is 10 to 15 mg daily and in giant cells arteritis 40 to 60 mg o.d. Relapses are common if therapy is stopped abruptly. After good clinical response prednisolone should be reduced and tapered off. Sometimes a small maintenance dose 5-10 mg may be required on a long term basis – even upto 3-5 years.

In ankylosing spondylitis long-term corticosteroids should not be given, but pulse doses may be needed to give relief in the active disease which does not respond to NSAIDs and other drugs.

Local Administration of Corticosteroids

Corticosteroids may be given by intra-articular injection to relieve pain and to increase mobility in rheumatoid arthritis with mono-or pauci articular involvement. Other diseases include tennis elbow, golfer's elbow, compression neuropathies and soft tissue inflammations such as fibrositis. Hydrocortisone acetate or one of the synthetic analogues such as triamcinolone hexacetonide is generally used.

P/A: Injection: Dexamethasone sodium phosphate 4mg/mL (I.P)
Hydrocortisone acetate 100mg/mL (I.P)
Triamcinolone acetate 10mg/mL (I.P)

Dose: Dexamethasone 4 mg/mL, intra-articular or intrasynovial injection 0.4 - 4mg. If required

injection is repeated at intervals of 3 - 21 days.

Hydrocortisone intra-articular or intrasynovial injection 5-50 mg.

Triamcinolone intra-articular or intrasynovial injection 5-40 mg.

Cost :

Dexamethasone :	Inj	4 mg/mL	(2 mL) Rs. 9.00 – 12.00
Hydrocortisone :	Inj	100 mg	(vial) Rs. 31.00 – 33.00
Triamcinolone :	Inj	40 mg/mL	(1 mL) Rs. 25.00 – 37.00
	Inj	10 mg/mL	(1 mL) Rs. 11.00 – 20.00

8.2.3 DRUGS WHICH SUPPRESS THE RHEUMATIC DISEASE PROCESS

Many drugs such as gold salts, penicillamine, hydroxychloroquine, chloroquine, immunosuppressants, and sulphasalazine suppress the disease process especially in rheumatoid arthritis and other forms of chronic arthritis. They are known as disease-modifying antirheumatic drugs (DMARDs). Unlike

NSAIDs which only relieve symptoms, DMARDs relieve the pathology. They do not produce immediate therapeutic effects but take a few weeks to several months for giving full response. Therefore they should be tried for upto six months if there are no adverse side effects before discarding them as ineffective.

Parenteral gold salts

Sodium Aurothiomalate

- I: Active progressive rheumatoid arthritis. With the availability of more effective and less toxic DMARDs is used only in exceptional circumstances.
- C/I: Renal and hepatic diseases, history of blood dyscrasias, exfoliative dermatitis, systemic lupus erythematosus, pregnancy and breast-feeding, past history of adverse reactions to gold salts.
- P/C: Patients should report pruritis, metallic taste, fever, sore throat, epistaxis, bleeding gums, jaundice, oedema and oliguria .
- S/E: Severe reactions may develop in upto 15% of patients. These include oral ulcers, skin reactions including severe exfoliative dermatitis, proteinuria, agranulocytosis, peripheral neuropathy, hepatitis and cholestatic jaundice.
- P/A: Injection 5, 10, 20, 25, 50 mg/mL
- Dose: By deep i.m. injection after the test dose of 10 mg initially, this is followed by weekly doses of 50 mg or more until there is definite evidence of remission. In most cases benefit is evident where a total dose of about 300 to 500 mg has been given. If there is no remission even after 1 g it should be discontinued.
- D/I: It increases the toxicity of myelosuppressive drugs. Blood levels of phenytoin are increased.
- Cost: Not freely available.

Aurothioglucose

- P/A: Injection 50 mg/mL
- Dose: First dose, 10 mg; second and third doses, 25 mg; fourth and subsequent doses, 50 mg. Continue the 50 mg dose at weekly intervals until 0.8 to 1 g has been given.
- Cost: Not freely available.

Oral gold salts

Auranofin

This is a hydrophobic gold containing compound, 25% of which is absorbed from GIT.

- I: Active progressive rheumatoid arthritis when NSAIDs alone are inadequate and in exceptional circumstances.

8. Analgesics and Antiinflammatory Agents

C/I, P/C: Same as for sodium aurothiomalate but in a milder degree

S/E: Diarrhoea, blood dyscrasias, allergy.

P/A: Tablets 3 mg.

Dose: 6-9 mg /day, starting initially in 2 divided doses, later as a single dose if needed. The dose may be increased to 9 mg daily in 3 divided doses over a period of 3 - 6 months if the response is inadequate. The drug has to be discontinued if it is ineffective even after 3 months on full dose.

D/I: Similar to sodium aurothiomalate

Cost: Tab 3 mg (10) Rs. 115.00 - 116.00

Penicillamine ☆

This has got immunosuppressive and metal chelating properties.

I: Active progressive rheumatoid arthritis, it is also a chelating agent which will eliminate copper, gold and probably other metals. It is also used in Wilson's Disease.

C/I: Hypersensitivity; lupus erythematosus

S/E: Initially nausea, anorexia, fever and skin reactions; loss of taste, blood disorders including thrombocytopenia, agranulocytosis and aplastic anaemia, rarely haematuria, myasthenia gravis Stevens - Johnson syndrome.

P/A: Capsules 250 mg

Tablets 50 mg, 125 mg, 250 mg.

Dose: Adult 125-250 mg o.d. before food for 1 month increased by similar amounts of intervals of dose should not exceed 4 weeks upto usual maintenance of 500-750 mg o.d. in divided doses. The maximum 1.5 g o.d.;

Elderly : initially up to 125 mg o.d. to a maximum of 1 g o.d.;

Children initial dose 50 mg o.d. before food for 1 month, increased at 4 week intervals to a maintenance dose of 15-20 mg/kg o.d.

D/I: Antacids, iron salts and zinc salts will reduce the absorption of penicillamine

Cost: Cap 250 mg (10) Rs. 65.00

Chloroquine Sulphate ☆

Though the main use of this drug is in the treatment and prophylaxis of malaria, chloroquine has anti-rheumatoid activity and are better tolerated but less powerful than gold or penicillamine. On long term use chloroquine gets deposited in the cornea and retina. Corneal deposits resolve on withdrawing the drug but the retinal lesions progress. So it is essential to examine the cornea and fundus in patients on long term therapy.

I: Active rheumatoid arthritis including juvenile arthritis, systemic and discoid lupus erythematosus and protozoal infections such as malaria, amoebiasis and giardiasis.

- C/I: Hypersensitivity, suspected resistance of *P.falciparum* infection, porphyria, retinal damage and use of concurrent hepatotoxic drugs.
- P/C: Hepatic and renal impairment, pregnancy, psoriasis, neurological disorders such as epilepsy and myasthenia gravis, severe gastrointestinal disorders and concurrent use of hepatotoxic drugs and ocular toxicity.
- S/E: Gastro-intestinal disturbances, headache, convulsions, visual disturbances, irreversible retinal damage, depigmentation or loss of hair, skin reactions such as rashes and pruritus, ECG changes, rarely blood dyscrasias.
- P/A: Tablets: chloroquine phosphate 250 mg
(equivalent to 150 mg base)
chloroquine sulphate 200 mg (equivalent to 150 mg base)
Syrup: chloroquine phosphate 80mg/5mL
(equivalent to 50 mg base/ 5 mL)
Injection: chloroquine hydrochloride i.v.
(equivalent to 40 mg base/mL) ,
chloroquine phosphate i.m. (equivalent to 40 mg base/mL)
- Dose: Rheumatoid arthritis Adults: Chloroquine base 150-mg b.d. or t.d.s.; maximum 2.5mg/kg/day,
Children up to 3mg/kg o.d.
(200mg of chloroquine sulphate or 250 mg of chloroquine diphosphate is equivalent to 150 mg of chloroquine base).
- D/I : Antacids reduce the absorption. Chloroquine antagonises the effects of neostigmine and pyridostigmine. Cimetidine inhibits metabolism of chloroquine and therefore varies the serum levels of the latter.
- Note: *For the prophylaxis and treatment of malaria the doses and routes of administration are different. For parenteral use chloroquine hydrochloride is available for i.v. infusions. This is indicated in severe malaria in areas where the organisms are not resistant. Chloroquine phosphate can be given i.m.*

Cost :	Tab	250 mg	(10)	Rs. 9.00 - 10.00
	Susp	100 mg/10 mL	(60 mL)	Rs. 7.00 - 13.00
	Inj	40 mg/mL	(5 mL)	Rs. 2.00 - 5.00

IMMUNOSUPPRESSANTS

Immunosuppressants have disease modifying activity in rheumatoid diseases. Azathioprine, methotrexate, cyclosporine and cyclophosphamide are used for this purpose in cases that do not readily respond to the common antirheumatic drugs.

Azathioprine ✧

- I: As an immunological suppressant in immunological mediated diseases.

8. Analgesics and Antiinflammatory Agents

C/I: Immuno suppressed states, hypersensitivity, previous treatment with alkylating agents, pregnancy and lactation.

P/C: Do blood counts once weekly for one month, then once a month to detect neutropenia and thrombocytopenia.

S/E: Nausea, vomiting, diarrhoea and precipitation of herpeszoster

P/A: Tablet 50 mg

Dose: 1.5 to 2.5 mg/kg daily in divided doses.

D/I: Allopurinol enhances the effect with increased toxicity

Cost: Tab 50 mg (10) Rs. 60.00 – 89.00

Methotrexate ☆

I: This is an antimetabolite mainly used for the treatment of leukaemias and cancers. As maintenance therapy for rheumatoid arthritis it has several advantages.

C/I: Renal impairment

P/C: Children, GI disorders, CNS disturbances, myelosuppression. Reduce the dose in hepatic or renal impairment and bone marrow depression. Monitor hepatic, renal and haematological parameters.

S/E: Nausea, vomiting, diarrhoea, anaphylaxis, hepatic necrosis, pulmonary fibrosis, fever, bone marrow depression, osteoporosis, menstrual dysfunction, cirrhosis, renal toxicity.

P/A: Tablets 2.5 mg

Injection 2.5, 5, 25, 250 mg/mL

Dose: Oral 7.5 mg – 10 mg single dose twice a week for maintenance therapy of rheumatoid arthritis. It should be started at a dose of 5-7.5 mg orally once a week. It may be increased in steps upto a maximum of 15 mg/week given in one or two doses.

Note: Blood counts should be done monthly to recognize leucopenia and thrombocytopenia. Liver enzymes (SGPT) should be done at intervals of 3-6 months to identify hepatic damage.

D/I: Aminoglycosides decrease absorption of oral methotrexate. Folic acid or its derivatives decrease the response to methotrexate. NSAIDs increase the plasma levels of methotrexate even to fatal levels. Presence of food in the stomach reduces the absorption of methotrexate.

Cost: Tab 2.5 mg (10) Rs 16.00- 36.00

Inj 50mg (2mL) Rs 52.00- 94.00

Cyclosporin ☆

I: This is a powerful immunosuppressant mainly used to prevent graft rejection after organ transplantations. It can be tried in resistant cases of rheumatoid disease and psoriasis not responding to conventional therapy.

C/I: Hypersensitivity to cyclosporin.

P/C: Epilepsy

S/E: Nephrotoxicity, hypertension, tremor, seizures, increased incidence of infections, headache, gynaecomastia, conjunctivitis, gingival hyperplasia, hirsutism, flushing, paraesthesias, tinnitus.

P/A: Capsules 25 mg, 50mg.

Injection 100 mg/mL 50 mL

Dose: Oral: 2.5 mg/kg/day in divided doses, if necessary increase gradually after 6 weeks upto a maximum of 4mg/kg. If there is no benefit after three months of therapy this drug should be discontinued.

D/I: Aminoglycosides, ciprofloxacin, co-trimoxazole and amphotericin increase the risk of nephrotoxicity. Phenobarbitone, phenytoin and primidone accelerate its metabolism. Progestogens inhibit metabolism. Potassium sparing diuretics increase the risk of hyperkalaemia.

Note: *Drugs like cyclosporine should be used only in institutions where facilities for titration of the dose, identification of toxic side effects and monitoring of blood levels are possible.*

Cost : Caps 25 mg (30) Rs. 585.00 - 690.00

Inj 100 mg/mL (50 mL) Rs.6000.00 - 6170.00

Cyclophosphamide ☆

I: This is an alkylating agent widely used for the management of several malignancies and also for immunosuppression in several immune-mediated diseases including rheumatoid arthritis.

Dose: Oral 1 to 1.5 mg/kg daily for rheumatoid arthritis with severe systemic manifestations, where other drugs have not been successful.

Parenteral: Given on a short-term basis i.v. in a dose of 0.5 to 1 g for severe systemic rheumatoid arthritis and for other connective tissue diseases especially those with active vasculitis. Regular blood counts should be carried out to detect leucopenia.

Cost : Tab 50 mg (10) Rs. 35.00

Inj 200 mg (vial) Rs. 35.00

8.2.4 DRUGS USED FOR GOUT

Gout is a metabolic disorder characterized by hyperuricaemia. Uric acid which is a product of purine metabolism accumulates with deposition in joints, kidneys, subcutaneous tissue and several other tissues. Acute gout which is a very painful condition is best treated with high doses of NSAIDs or colchicine (if it is available) whereas chronic gout is managed by drugs which lowers serum uric acid levels either by suppressing its production or eliminating it in urine (uricosuric drugs). Drugs used for chronic gout may not be successful for treating the acute attack, they may even worsen the condition.

8. Analgesics and Antiinflammatory Agents

Acute attack: Acute attacks of gout are usually treated with high doses of NSAIDs eg: Indomethacin, naproxen or piroxicam. Colchicine is an alternative.

Colchicine

I: Colchicine is neither an analgesic nor an anti-inflammatory, but it specifically suppresses gouty inflammation. It does not inhibit the synthesis or promote the excretion of uric acid. Thus it has no effect on blood uric acid levels.

C/I: Pregnancy and lactation.

P/C: Elderly, gastro-intestinal disease, cardiac, hepatic and renal impairment.

S/E: Nausea, vomiting, and abdominal pain, diarrhoea, gastro-intestinal haemorrhage, rashes, renal and hepatic damage.

P/A: Tablet 0.25 mg, 0.5 mg

Dose: 1 mg initially, followed by 0.5 mg every 2-3 h until relief of pain is obtained, or until a total dose of 10 mg has been reached. The course should not be repeated within 3 days, once the acute attacks are controlled.

Prevention of further attacks is by using allopurinol or uricosuric drugs. Colchicine also may be used in doses 0.5 mg b.d. or t.i.d.

Cost: Tab 0.5 mg (10) Rs. 9.00 – 10.00

Chronic Gout

Allopurinol ☆

I: This reduces the production of uric acid in the body and therefore is used for prophylaxis of gout and of uric acid and calcium oxalate renal stones.

C/I: Ineffective in acute gout but useful for prevention of further attacks. It is useful in gout and also in conditions where anticancer drugs are used in leukaemias and lymphomas where large scale cell-kill is effected with consequent hyperuricaemia.

P/C: Administer prophylactic NSAIDs, but not aspirin or salicylates for at least 1 month after hyperuricaemia is corrected. Ensure adequate fluid intake (2L or more daily). Monitor for hepatic and renal impairment.

S/E: Rashes, fever, lymphadenopathy, arthralgia, eosinophilia, gastro-intestinal disorders, hypertension, alopecia, hepatotoxicity and neuropathy.

P/A: Tablets 100 mg

Dose: Initially 100 mg o.d. as a single dose, after food, gradually increased to 300 mg or more o.d. depending on the serum uric acid levels. Usual maintenance dose is 100-300 mg /day, rarely upto 900 mg.

D/I: Allopurinol enhances anticoagulant effects of coumarin drugs and warfarin. Effects of azathioprine, cyclophosphamide and mercaptopurine are enhanced with increased toxicity.

Cost : Tab 100 mg (10) Rs. 12.00 – 13.00

Probenecid

- I: This is a uricosuric drug which helps elimination of uric acid in urine and therefore indicated in chronic hyperuricemia. Also used for the prophylaxis of exacerbations of gout. It also reduces the tubular excretion of penicillins and some of the cephalosporins and therefore used along with them to raise their blood levels.
- C/I: History of blood dyscrasias, nephrolithiasis, porphyria and acute gout attack; avoid the concurrent use of probenecid with aspirin and salicylates.
- P/C: During initial gout therapy administer prophylactic colchicine or NSAIDs, ensure adequate fluid intake; and render the urine alkaline to prevent the crystallisation of uric acid, peptic ulceration, renal impairment.
- S/E: Gastro-intestinal disturbances, urinary frequency, headache, alopecia, hypersensitivity, dermatitis, Stevens-Johnson syndrome, nephrotic syndrome and aplastic anaemia.
- P/A: Tablets 500 mg.
- Dose: For uricosuric therapy, start initially with 250 mg b.d. after food, and increase to 500 mg b.d. in a week, then up to 2 g daily in 2-4 divided doses depending upon the plasma - uric acid concentration. For maintenance dosage, smaller doses are continued.
- D/I: Aspirin antagonises its effect. Probenecid reduces the urinary excretion of several drugs including indomethacin, ketoprofen, naproxen, beta lactum antibiotics, captopril, acyclovir, zidovudine and methotrexate, leading to raised serum levels of those drugs and toxicity. There is antagonism between probenecid and pyrazinamide.
- Cost : Tab 500 mg (10) Rs. 25.00

8.2.5 DRUGS USED FOR THE RELIEF OF SOFT-TISSUE INFLAMMATION

Hyaluronidase

- I: This enzyme enhances the permeation of subcutaneous and intramuscular injections, local anaesthetics, and s.c. infusions. It promotes the resorption of inflammatory oedema and haematomas.
- C/I: Do not apply directly to cornea. Avoid sites where there is active malignancy. Hyaluronidase should not be given i.v.
- P/C: Infants and elderly
- S/E: Occasional severe allergy.
- P/A: Vial 1500iu /mL.

8. Analgesics and Antiinflammatory Agents

Dose: 1500 units dissolved in solution to be injected s.c. or i.m. For local anaesthesia 1500 units mixed with 20 mL of the anaesthetic solution. Hypodermoclysis i.e. s.c. injection of a saline or other solution, 1500 units dissolved in 1 mL water for injection or 0.9% sodium chloride injection is administered before start of the infusion fluid. Upto 500-1000 mL of infusion fluid can be administered through this route.

For the resolution of drug extravasation and haematomas, 1500 units dissolved in 1 mL of water for injection or 0.9% sodium chloride are infiltrated locally over the affected site.

Cost : Vial 1500 iu (1 mL) Rs. 18.00 – 19.00

8.2. 6 RUBEFACIENTS AND OTHER TOPICAL COUNTER IRRITANTS

Rubefacients act by counter-irritation. Counter-irritation is comforting in painful lesions of the muscles, tendons, and joints and in non-articular rheumatism. Drugs such as NSAIDs can be administered in transdermically absorbable form for local anti-inflammatory action. Rubefacients cause local vasodilatations which may help to resolve local inflammations. Several drugs are used eg. methyl salicylate (oil of wintergreen), turpentine, capscicine and others. Most of them are over the counter drugs and popular household remedies for sprains and myalgia.

Topical NSAIDs may provide some slight relief of pain in musculoskeletal conditions. These should be applied with gentle massage. Avoid contact with eyes, mucous membrane and inflamed and broken skin. Discontinue if rashes develop. They are not to be used with occlusive dressings. Not generally suitable for children.

CHAPTER 9 : DRUGS ACTING ON BLOOD AND BLOOD FORMING ORGANS

9.1 NUTRITIONAL ANAEMIAS

9.1.1 Iron deficiency anaemia

Iron deficiency is the commonest haematological disorder in all parts of India.

Drugs used in iron deficiency

Iron preparations, oral and parenteral.

9.1.2 Megaloblastic anaemia

Folic acid 1 mg /day orally

In severe cases 5 mg /day orally

Vit B12 10 mcg /day orally

In severe cases 1 mg (1000 mcg) i.m. injection once in 3 days for 4-5 doses followed by oral administration)

Pernicious anaemia, post gastrectomy states, malabsorption syndromes.

Vit B12 i.m. injections as needed.

Prophylaxis of megaloblastic anaemia during anticonvulsant therapy:

100 mcg folic acid /day orally.

9.2 HAEMOLYTIC ANAEMIAS

9.2.1 Acquired haemolytic anaemias

Autoimmune haemolytic anaemia

1. Glucocorticoids: Mainstay of treatment consists of the administration of glucocorticoids.

P/A: Prednisolone 5 mg tab

Triamcinolone 4 mg tab

Dexamethasone 0.5 or 1 mg tab

Betamethasone 0.5 or 1 mg tab

For mild cases and for prolonged treatment, oral preparations are preferred - dose equivalent of 1-2 mg/kg/bw prednisolone to start with, later tapered to the lowest maintenance dose.

Treatment may have to be continued for prolonged periods, in many cases, for decades.

9. Drugs Acting on Blood and Blood Forming Organs

For more acute haemolytic crisis:

1. Parenteral steroids : i.v. hydrocortisone 100 mg 8 h or more frequently if needed. Larger doses are given through i.v. infusion, maintained for varying periods, the rate being adjusted depending on the clinical condition. Betamethasone and dexamethasone can be given parenterally in doses of 4-8 mg i.v. or i.m. 8 h or as continuous i.v. drip.

In severe cases not responding to the maximum tolerated doses of corticosteroids methyl prednisolone 1 g i.v. infusion once a day, up to 3 days is highly effective.

2. Immunosuppressants

These act as adjuvants to glucocorticoids to bring about better immune suppression and help to reduce the dosage of corticosteroids. During the acute phase.

Azathioprine

P/C : Monitoring of the blood counts weekly and hepatic and renal function tests monthly.

S/E : Bone marrow suppression and hepatic and renal impairment, hypersensitivity reactions, hair loss, increased susceptibility to infections and pancreatitis.

Dose : 1 - 2 mg/kg bw orally, later to be tapered off.

Cyclophosphamide

Used as an adjunct in immunosuppression therapy

I : Treatment of leukaemias, lymphomas and solid tumours.

C/I : Bladder haemorrhage, pregnancy, lactation, leucopenia, thrombocytopenia.

P/C : Infection, blood disorders.

S/E : Bone marrow suppression, haemorrhagic cystitis characterized by dysuria, haematuria and other lower urinary tract symptoms.

P/A : Tablets 50 mg,

Injections 200, 500, 1000 mg

Dose : 1- 2 mg/kg bw

Injections to be reconstituted and given i.v. slowly or in a drip to run over 1 hour .

D/I : Toxicity of cyclophosphamide is aggravated by allopurinol, Cyclophosphamide enhances the effect of suxamethonium.

Cost : Tabs 50 mg (10) Rs. 22.00 - 35.00

Inj 100 mg (vial) Rs. 19.00 - 22.00

9.2.2 Drug induced haemolytic anaemia

Several drugs cause haemolysis by different mechanisms such as direct damage to erythrocytes, interference with their metabolic pathways especially in the presence of enzymopathies, or immunological mechanisms eg : penicillin, alphanemethyl dopa, stibophen, INH, PAS, sulpha groups of drugs, and others. The haemolysis may be mild and subclinical or may be fulminant presenting as rapidly developing anaemia and haemoglobinuria. It is therefore advisable to monitor patients who are receiving these drugs on long-term basis for the development of haemolysis.

Acute episodes are treated by

1. Drug withdrawal.
2. Close monitoring.
3. Fluid and electrolyte replacement to avoid shock and renal failure.
4. Other supportive measures.

Such persons and their family members should be informed of the risk of recurrence in future.

9.2.3 Haemolytic disease of the newborn

Once detected or suspected, the mother and child should be directed to a centre with facilities for expert paediatric and haematology services. Treatment of the established case is as follows :

Children

1. Close monitoring of haemoglobin, glucose and unconjugated bilirubin.
2. Observe the clinical status of the patient.
3. When the serum level of bilirubin rises above 20 mg/dL in full term babies or 15 mg/dL in premature babies, exchange transfusion with washed group D Rh-ve erythrocytes is indicated. By exchange transfusion antibody coated erythrocytes and bilirubin are removed from circulation. Usually 150 mL of whole blood/kg bw is the requirement for an exchange.

Other forms of therapy include phototherapy using direct sunlight or ultraviolet light and phenobarbitone which is an enzyme inducer in the liver. Dose 30-60mg/day. Women with history of Rh incompatibility should receive proper antenatal management in subsequent pregnancies in order to avoid foetal loss and permanent morbidity for the body. Depending the severity of affection of the foetus intraperitoneal transfusion of Rh-ve blood or even direct i.v. infusion has to be undertaken.

If the risks to the baby are high, premature termination of pregnancy has to be undertaken.

Rh -ve mothers who are at risk of having Rh +ve babies i.e. those whose husbands are Rh +ve and those who develop Rh -D antibody titres

9. Drugs Acting on Blood and Blood Forming Organs

during pregnancy should be given anti-D gamma globulin 300 mcg within 72 h of a delivery, abortion, ruptured ectopic gestation or amniocentesis. Anti-D immunoglobulin is given i.m.

P/A: Human anti-D immunoglobulin vials containing an enriched fraction of antibodies against the D-antigen.

Cost : 300 mcg 1.5 mL vial Rs 2475.00

9.2.4 Symptomatic haemolytic anaemias

These occur in several conditions such as disseminated lupus erythematosus, autoimmune disorders, dysproteinaemias, parasitic infections such as malaria and the like. Treatment is directed towards the primary condition. If haemolysis is severe, transfusion of packed cells, supportive measures to prevent renal failure, immunosuppressants and plasmapheresis to remove immunoglobulins are indicated.

9.2.5 Paroxysmal nocturnal haemoglobinuria

Treatment is supportive. If haemolysis is severe, transfusion of washed erythrocytes may be necessary.

9.2.6 Inherited enzyme deficiencies leading to haemolytic anaemias

The most common condition coming under this group is glucose - 6 - phosphate dehydrogenase (G6PD) deficiency, which is prevalent in many communities in India. Several genetic variants are present. When the enzyme level is 10 - 60% of normal, haemolysis occurs when exposed to several drugs such as antimalarials, sulpha groups of drugs, analgesics, several other groups of drugs and certain foods such as fava beans. If the enzyme level is below 13% of normal spontaneous haemolysis occurs. Once these subjects are identified, they and their family members should be warned about the possible ill effects of several drugs. If haemolytic episodes occur, withdrawal of the offending drugs and supportive care with large intake of fluids to avoid renal failure, transfusion of fresh erythrocytes and other symptomatic measure should be instituted. They should be warned about the possible adverse reactions to future medication.

9.3 HYPOPLASTIC AND APLASTIC ANAEMIAS

These are encountered rarely in general practice. In 25 % of them a cause may be obvious. Identifiable causes include drug toxicity, irradiation, viral infections such as human parvovirus 19, hepatitis virus, aplastic crisis in haemolytic anaemias, pregnancy, thymomas, paroxysmal nocturnal haemoglobinuria, chronic renal failure and others. In children congenital aplastic anaemia (fanconi's) forms an identifiable group. About 50 % have an immunological basis and these respond to immunomodulatory drugs. The modifications include anabolic steroids, corticosteroids, immunosuppressants, pyridoxine, antilymphocyte

globulin or antithymocyte globulin, erythropoietin and others. Bone marrow transplantations has to be considered in those cases which are not suitable for drug treatment and for those who are non-responsive to them.

9.3.1 Anabolic steroids

Nandrolone decanoate, oxymethelone

I: Fanconi's anaemia, mild to moderate aplastic anaemia in adults.

C/I: Cardiac failure, hepatic failure, androgen dependent tumours.

P/C: Cardiac or renal impairment, circulatory failure, hypertension, diabetes mellitus.

S/E: Weight gain, virilization, fluid retention, cholestatic jaundice and others.

P/A: Nandrolone decanoate injection - 25 mg, 50 mg, 100 mg.

Oxymethelone tablets 5 mg, 50 mg

Dose: Nandrolone decanoate 50 - 100 mg i.m. weekly. Due to the low platelet count bleeding at injection site may occur.

Oxymethelone: oral 2 - 3mg/kg/bw given, daily for 2 - 3 months.

D/I: Anticoagulant effect of nicoumalone, phenindione and warfarin enhanced.

Cost: Nandrolone decanoate inj 25 mg (1 mL) Rs. 45.00 - 50.00

Oxymethelone tab 5 mg Rs. 260.00

Corticosteroids: These are partly beneficial in a small proportion of cases especially in drug induced aplastic anaemia, if given in the early stages. The dose range is 1 - 2 mg/kg bw of prednisolone orally given for varying periods. In acute aplastic crisis occurring in the course of haemolytic anaemias methylprednisolone given as i.v. infusion in a dose of 1 g/day for 3 - 4 days may tide over the crisis.

9.3.2 Immunosuppressants:

Azathioprine given in a dose of 1 - 2 mg/kg bw along with corticosteroids is beneficial in a small proportion. More potent immunosuppressants such as cyclosporine in a dose of 2 - 6 mg/kg bw. Orally daily for varying periods are more effective.

Cyclosporine

S/E: Dose dependant increase in serum creatinine and urea, later on going to renal structural damage, hypertrichosis, tremors, hypertension, gastrointestinal disturbances, hyperkalemia, hyperuricemia, predisposition to malignant lymphomas on long term administration, and others.

In resistant cases antithymocyte serum (15 mg/kg bw i.v. for 8 days) or large doses of immunoglobulin (sandoglobulin sandoz, NLI

9. Drugs Acting on Blood and Blood Forming Organs

in a dose of 400 mg/kg bw daily as i.v. infusion for five days followed by subsequent courses depending upon the response produces benefit.

Note: *Aplastic anaemia of any severity is a serious condition which demands careful expert management by a trained team in tertiary care hospitals and therefore such cases have to be referred to those centers for optimal benefit.* For drug resistant cases bone marrow transplantation is the curative option.

Erythropoietin

I: Hypoplastic anaemia accompanying chronic renal failure (CRF)

This responds satisfactory to erythropoietin injections. Along with improvement in haemoglobin levels the need for dialysis, haemorrhagic tendency and renal function also improve in many cases.

C/I: Uncontrolled hypertension, hypersensitivity to mammalian cell products, hypersensitivity to human albumin.

P/C: CRF, ischaemic heart disease, hypertension, pregnancy.

S/E: Rise in blood pressure, hypertensive encephalopathy, thrombocytosis, flu-like symptoms, anaphylaxis and others. Interaction with ACE inhibitor leads to hyperkalemia.

P/A: Recombinant human erythropoietin: (Epoietin alpha and beta)

Inj 2000 iu/mL, 4000 iu/mL

Dose: Erythropoietin 2000 unit / mL given s.c. or as i.v. injection over 2 minutes. 50 unit/kg bw given thrice a week to start with. The dose is increased by 25 units/kg at intervals of 4 weeks, in order to achieve the optimum haemoglobin levels, up to a maximum of 600 mg/kg bw weekly in 3 divided doses.

Dose is to be adjusted so that the haemoglobin level rises at a rate of 2 g/dL every month till it reaches a stable level of 10 - 12 g/dL.

D/I: None reported

Cost: Inj 2000 iu (2 mL) Rs. 1700.00

9.4 HAEMOGLOBINOPATHIES

Several haemoglobinopathies have been described from India. These include haemoglobins D, E, F, H, I, J, K, L, M, S, Q. Norfolk, Lepore and possibly others. Among these, haemoglobin S, E, D, J, K, and Q have been studied in greater detail including prevalence studies in many areas. HbS and E are widely prevalent, the former in many parts of India among tribals and other communities, the latter in the eastern states of West Bengal and Assam.

9.4.1 Sickle cell anaemia

Management includes :

- a. Long term management to prevent deterioration and crisis and
- b. emergency management of crisis.

The long term management consists of hypertransfusion to keep haemoglobin levels 12-14 g / dL and use of iron chelating agents prophylactically and / or therapeutically to avoid iron overload.

If available, bone marrow transplantation should be advised early.

Long term penicillin prophylaxis is instituted to avoid recurrent pneumococcal infection which leads to crisis. Phenoxymethyl penicillin (pencillin-V potassium) is given in a dose of 125 mg b.d. orally. This regimen is started before the age of four months.

Polysaccharide pneumococcal vaccine should be given early in life to prevent subsequent severe pneumococcal infections.

Hydroxyurea helps to reduce the frequency and severity of sickling and crisis. The dose is 500 mg b.d. oral.

Folic acid - 1 mg given daily prevents the development of folate deficiency which is a common accompaniment.

Emergency management of crisis

Rest, sedation with phenobarbitone 60 mg or diazepam 5 - 10 mg orally.

Adequate intake of fluid and electrolytes to prevent dehydration. If the haemoglobin falls rapidly transfuse packed cell.

Opioid analgesics such as dextropropoxyphene, pentazocine or pethidine to relieve pain.

9.4.2 Sickle cell trait

Genetic counselling should be given. Birth of affected children should be avoided by intervention in pregnancies carrying affected foetuses.

9.4.3 Thalassemias

These are also prevalent in a large scale in many communities in India. In Kerala it is seen sporadically in several families. Thalassaemia major is associated with severe clinical manifestation of haemolytic anaemia, and untreated, most of the children die before or after reaching adolescence. In thalassaemia intermedia and thalassaemia minor the clinical manifestations are milder and these are compatible with longer life and reproduction. It is therefore essential to investigate all members of such families fully in haematology centres so as to identify all affected subjects and institute proper care.

In the case of thalassaemia major it is ideal to put them on super transfusion therapy from early life with the aim of maintaining the haemoglobin around 12g/dL, along with iron chelating therapy.

Bone marrow transplantation is an attractive option for those who can

9. Drugs Acting on Blood and Blood Forming Organs

afford and who have compatible donors. Cost of bone marrow transplantation in India is around Rs. 7,00,000-10,00,000. Drugs used in thalassemias include hydroxyurea in a dose of 500 - 1000 mg b.d. orally, cytosine arabinoside given i.v. or i.m. in different dosages and 5 - azacytidine (50 - 400 mg /m² body surface daily for 5 days). These drugs help to elevate the content of foetal haemoglobin, and thereby reduce the clinical severity of the disease.

9.4.3.1 Heterozygous thalassemia (Thalassemia minor)

Essentials of therapy consist of strict avoidance of medicinal iron, genetic counselling and iron chelation therapy when indicated.

There are thalassemia societies in India which undertake to disseminate information to members of affected families and also help to procure treatment.

9.4.3.2 Thalassemia syndromes

These also exist in a large way in many communities in India. In these conditions genes for abnormal haemoglobins and thalassemias are present in a double heterozygous manner so that their haemoglobin pattern is a mixture of foetal haemoglobin and the abnormal haemoglobin. eg. Hb S - thalassemia, Hb- E thalassemia etc. These are milder clinically compared to thalassemia major and their treatment is symptomatic. Genetic counselling is necessary.

9.5 IRON CHELATING DRUGS

These are indicated when the body stores of iron are increased to abnormal levels giving rise to damage to organs like the heart, liver, pancreas and others. Iron overload occurs spontaneously in haemochromatosis. Repeated blood transfusions given to patients with thalassemic syndromes and sickle cell anaemia without simultaneous iron chelation therapy leads to iron overload. Parenteral administration of iron preparations if given in excess of actual requirement will lead to abnormal accumulation of iron in tissues. A simple biochemical marker for the estimation of storage iron in the body is the serum ferritin levels. Values above 500 mcg/L should suggest abnormal iron accumulation requiring the use of chelating agents.

Desferrioxamine

It is a useful iron chelating agent.

I: To prevent and treat iron overload in conditions requiring frequent and repeated whole blood or packed red cell transfusions, haemochromatosis, haemosiderosis, acute toxicity by overdose of medicinal iron, aluminium overload in chronic haemodialysis patients.

C/I: Renal impairment

P/C: Impaired renal function, children below 3 years, increased susceptibility to infection, pregnancy and lactation.

S/E: Gastrointestinal disturbances, hepatic and renal damage.

anaphylaxis, arrhythmia, hypotension, blurring of vision and local reactions at the site of injection.

P/A: Injection 500 mg / vial

Dose: 20 - 40 mg/kg/bw daily given as a s.c. infusion overnight or along with the blood transfusion.

This has to be repeated 4-5 times a week indefinitely as long as transfusion therapy is needed.

D/I: Antipsychotic drugs administered concurrently may lead to adverse interaction. Vit C enhances the urinary elimination of iron and therefore acts synergistically.

Cost: Inj 500 mg / vial (5) Rs. 700.00

Deferiprone

It is an oral iron chelating drug which has undergone clinical trials and is available for use.

I: Iron chelation

P/C: Pregnancy and lactation.

S/E: Agranulocytosis, arthralgias, arthritis, drug induced lupus erythematosus, toxic overload of iron in the liver.

P/A: Tablets 250 mg, 500 mg.

Dose: 0.5 - 3 g daily (100 mg/kg bw) to be given 1 h before food, in three divided doses. Iron elimination is increased by concurrent administration of Vit C.

Cost: Tab 250 mg (50) : Rs. 475.00

9.6 DRUGS USED IN LEUKAEMIAS

Management of leukaemias is to be undertaken in haematology centres equipped with facilities for advanced investigations, and administration of intensive chemotherapy. In order to get best results the proper diagnosis has to be established and the most effective protocols are to be started from the beginning. Since many of the drugs are highly toxic and several invasive modalities of management have to be followed, it is essential that suspected cases are referred to specialized centres without delay. Moreover it is now established that improper and partial treatment given during the course of illness adversely affects the final outcome.

9.6.1 Chronic myeloid leukaemia

Busulphan

This is an alkylating agent.

I: Chronic myeloid leukaemia (CML)

C/I: Hypersensitivity, bone marrow depression, gout, myelodysplasia.

9. Drugs Acting on Blood and Blood Forming Organs

P/C : Frequent blood counts are necessary. Busulphan is cheap compared to other drugs and it is easy to administer. Due to the fact that patients initially treated with busulphan fare badly with bone marrow transplantation (BMT) this drug is not used as the primary treatment for CML at present.

Busulphan when given in larger doses predictably ablates haemopoietic cells in the bone marrow and therefore it is used in the preparation of the receipient for BMT.

S/E: Bone marrow aplasia if medication is continued indefinitely without regular blood counts, dark pigmentation, cataract, and pulmonary fibrosis.

P/A: Tablets 2 mg.

Dose : 2 - 8 mg/day in single or divided doses. Medication is started when the CML is diagnosed and it is stopped when the total leukocyte (TLC) comes down to 10000/cmm. The drug is restarted when the TLC goes up above 50000/cmm. Treatment is to be given intermittantly.

D/I: Cyclophosphamide enhances the haemopoietic toxicity, immunization with live viruses can cause life threatening infections.

Cost : Tab 2 mg (100) Rs.300.00 - 400.00

Hydroxy Urea

This is affective in reducing the TLC and relieving symptoms. Initial results are excellent and 80 - 90 % of patients respond. Treatment is given continuously starting with higher doses in order to reduce the TLC rapidly and thereafter continued at a lower maintenance dose in order to keep the TLC within normal limits and make the patient symptom free.

At present hydroxyurea is the drug of choice for initial therapy in those who cannot afford interferon.

I: CML, polycythemia vera, thalassemia.

C/I: Bone marrow suppression, pregnancy and lactation, severe anaemia.

P/C : Frequent blood counts are necessary, renal and hepatic function to be monitored

S/E: Myelosuppression, gastro intestinal upsets and allergic skin lesions.

P/A: Capsules of 250 mg, 500 mg

Dose : 20 - 30 mg/kg bw (1-4 g/day) in divided doses.

D/I: Concomitant use of cytarabine increases the risk of haematological toxicity, Immunization with live or attenuated vaccines can result in manifestation of infection.

Note : Both busulphan and hydroxyurea only supress the leukaemia without achieving cure. After varying periods of symptomatic relief, the disease enters the blastic phase at which both these drugs are ineffective.

Cost : Tab 500mg (10) Rs. 110.00

Interferon Alpha - (Previously known as leucocyte interferon)

This is an immunomodulatory and cytotoxic drug. It is useful in different types of haematological malignancies. Other actions include antiviral activity against several viruses.

In CML it induces relief in 80 - 90% of cases and may even bring about eradication of the abnormal clone in 10-15% of cases. So in patients who can afford the cost, this is the treatment of choice.

I: CML, hairy cell leukaemia, Hepatitis -B, Hepatitis- C, other immunemediated diseases Interferon can be combined with hydroxyurea given orally and/or cytosine arabinoside in a dose of 20 mg/m² / daily for 10 days. Combination therapy is more effective. It also reduces the requirement of interferon, and thus the cost of therapy.

C/I: Autoimmune disease, bone marrow depression, cardiac disease, diabetes mellitus, chicken pox, hepatic diseases.

P/C: Pregnancy and lactation.

S/E: Nausea, vomiting, febrile episodes resembling flu, polyneuropathy and psychosis.

P/A: Vials of 3 or 5 million iu.

Dose: 3-9 million units by i.m. or s.c. injection daily or in smaller doses at more wider intervals 3-4 times a week for several months, usually 4 - 6 months.

D/I: Enhances effect of theophylline.

Cost : Inj vial (3 million iu) Rs. 600.00 - 1000.00.

Cost of treatment for 1 year will be Rs.3,65,000.00

BMT

BMT is advanced for patients below the age of 50 years who have suitable compatible donors and who can afford the expense.

Once the disease enters the accelerated and blastic phases most of the drugs used in the CML phase become ineffective. So also the utility of BMT.

Interferon Beta

I: Relapsing multiple sclerosis, fibroblast interferon has also immunomodulating properties.

C/I: Major depression, suicidal tendencies, epilepsy, hepatic failure and myelosuppressive.

P/A: 300 mcg (9.6 million unit) vials for subcutaneous infection.

Dose : To be decided in individual cases

9. Drugs Acting on Blood and Blood Forming Organs

P/C :, S/E :, D/I : Similar to interferon alfa.

Cost : Not available.

9.6.2 Chronic lymphatic leukaemia

Drugs therapy is indicated when the disease is in stage 2 or more.

Chlorambucil

This is an alkylating agent

I : Chronic lymphocytic leukaemia, indolent non-hodgkins lymphomas, Hodgkins disease and ovarian carcinomas.

C/I : Lactation.

P/C : Leucopenia, thrombocytopenia, pregnancy, renal and hepatic dysfunction.

S/E : Hypersensitivity reactions, gastrointestinal upsets, bone marrow suppression and predisposition for second cancers - especially lymphomas.

P/A : Tablets 2 mg, 5 mg

Dose : 0.05 to 0.1 mg daily continuously till the TLC becomes normal and clinical features subside. Thereafter the drug may be stopped or continued in a lower dose as maintenance.

An alternate regimen is to give 0.4 kg/bw given thrice a week intermittently.

Corticosteroids

These may be used as adjuvant drugs. These enhances the antitumor effects of chlorambucil, as well as produce symptomatic improvement, when given on a short term basis.

Prednisolone Dose : oral 0.5 - 1 mg/kg bw daily.

Combination chemotherapy using cyclophosphamide, doxorubicin, vincristine and prednisolone is capable of bringing about relief in resistant cases.

Other modalities of treatment :

Splenic irradiation - 300 - 1000 cGy in divided doses.

Leukapheresis : This is the procedure to remove leucocytes from blood by using a cell separator - it brings about a temporary reduction in tumour load and also comets the hyperviscosity.

D/I : Potentiation of other nyelosuppressive agents, phenylbutazone and warfarin potentiates the effect of chlorambucil.

Cost : Tab 2 mg (25) Rs. 130.00

9.6.3 Acute leukaemias

They are broadly divided into acute lymphatic (lymphoblastic) leukaemia

(ALL) and acute non lymphatic leukamias (ANLL). These are further subclassified. ALL is subclassified into L1, L2, and L3 types depending on the cell morphology, surface immune markers and other characteristics. ANLL is further subclassified into seven groups M1 to M7 depending on the stage of differentiation of the progenitor stem cell. Other neoplasms which may present as leukaemia include lymphomas, (lymphosarcoma leukaemia) and multiple myeloma (plasma cell leukaemia).

Modern management which aims at cure in as high a proportion as possible, involves highly specialized investigations to delineate the cell morphology, immune markers, cytology, cyto-chemistry, genetic markers, chromosomal abnormalities and such others. The prognosis varies between the different subgroups, and depending upon the aggressiveness and biological behaviour several protocols for combination chemotherapy have been formulated. These have to be instituted from the beginning and continued without default in order to achieve the best results. Since most of the drugs are highly toxic and associated with severe side effects, their administration should be under strict supervision by a trained team. Moreover the problems of immunosuppression, nosocomial infections, haemorrhagic tendency and extreme psychological stress for the patient and his relatives complicate the management.

Some facility is available in Kerala in the Medical College Hospitals and Regional Cancer Centre, Trivandrum. It is therefore essential that primary care physicians refer cases of established or suspected leukaemias to those centres early during the course of the disease. Their involvement in such cases should be to provide home therapy under direction from the specialist, moral support and follow up.

Several drugs are used in the treatment of acute leukaemias.

These include :-

1. Antimetabolites : Methotrexate
Cytosine arabinoside
6-mercaptopurine
6 - thioguanine
2. Vinca alkaloid : Vincristine
3. Antibiotics : Daunorubicin - (Daunomycin)
Doxorubicin (Adriamycin)
Rubidazone
Bleomycin, Mitomycin.
4. Enzymes : L-asparaginase
5. Alkylating agent : Cyclophosphamide
6. Corticosteroids : Prednisolone and its analogues.
7. Vitamin analogues : All - trans retinoic acid.
8. Immunomodulators : Interferons.

9.6.4 Myelodysplastic syndrome

Drug therapy. Drugs which induce cell differentiation are employed

9. Drugs Acting on Blood and Blood Forming Organs

Cytosine arabinoside : low dosage 10 - 20 mg / m² / day

All transretinoic acid : Oral 0.5 - 1 mg daily

1.25 Cholecalciferol

Stimulators of myelopoiesis and differentiation

GM - CSF lenogastim - i.v. 10.2 million units / m² / daily till the total leucocyte count reaches normal.

9.6.4.1 Haematopoietic growth factors

These include granulocyte colony stimulating factor (G-CSF), granulocyte-macrophage colony stimulation factor, (G-MCSF) erythropoietin and several other cytokines which stimulate proliferation and differentiation of many normal cell lines during the course of development of the stem cell. These are prepared by recombinant DNA technology. Specific colony stimulating factors are indicated in the following conditions.

1: Drug induced cytopenias, post bone marrow - transplantation cytopenic states, organ transplantation, aplastic anaemia, agranulocytosis

Dose : Ranges from 5,00,000 units / kg bw i.v. daily till the desired effect is obtained.

These drugs are to be used only under specialist supervision.

Cost : Inj 300mcg (1mL) Rs.5200.00 - 5300.00

At present several other drugs are employed for managing leukaemias. These are beyond the scope of the State Drug Formulary, since they have to be used only in special situations under close monitoring by specialists.

9.6.5 Multiple myeloma

This condition is primarily treated with **melfhalan** (phenylalanine mustard), **prednisolone** and **cyclophosphamide** in various regimens.

Dose : Orally 2 mg daily for prolonged periods along with prednisolone 1 mg/kg bw.

Melphalan 2 to 4 mg daily and prednisolone 30 - 60 mg daily can be given as a continuous regimen until symptoms are relieved, myeloma protein band disappears and radiological clearance of bone lesions is achieved. There is an intermittent regimen which is claimed to be better.

Schedule : Melphalan 8 mg/m² orally for 4 consecutive days along with prednisolone 60 mg/m² orally.

This course is repeated once in four weeks. If the response is not satisfactory, the dose of both drugs may be raised by 20%.

Combination chemotherapy is indicated in those with poor response. Several protocols are available. A popular regimen is to give

.....contd on page-266

DISORDERS

9.7.1 Purpuras

Immuno thrombocytopenic purpura (ITP)

9.7.1.1 Acute ITP

Corticosteroids

Oral dose: These form the mainstay of drug therapy. Prednisolone is given orally in a dose of 1-2 mg/kg bw in 24 h - as divided doses. In the vast majority of cases the severity of bleeding comes down within 24 - 36 h.

Parenteral dose: Hydrocortisone hemisuccinate sodium 100 mg or betamethasone 8 mg should be given as an i.v. drip within 1- 2 h if the bleeding manifestations are more severe. If the bleeding continues, this has to be administered for 24 - 36 h as a continuous i.v. drip, the dose and rate of infusion being determined by the clinical state. Once the bleeding is controlled, the patient is put on oral prednisolone and followed up. In those who fail to respond to adequate dosage of corticosteroids, and if the condition is life threatening, emergency splenectomy may have to be undertaken.

Intravenous immunoglobulin (i.v. Ig)

This is normal immunoglobulin (i.v.Ig) available as Sandoglobulin.

I: Immune thrombocytopenic purpura, other indications include acute Guillain Barre syndrome, other immune mediated diseases

C/I: Allergic states.

S/E: Allergic reactions, fever, arthralgia, hyperviscosity states precipitating myocardial infarction and strokes in susceptible subjects.

Dose : In ITP administration of large doses 0.2 to 0.4 g/kg bw daily for 3 - 6 days brings about rapid remission of the bleeding and restores the platelet counts to normal in more than 70% of case. Immunoglobulin can be combined with corticosteroids with benefit. The effect of i.v.Ig is temporary, lasting for a few weeks. It is an excellent method to tide over an emergency.

IVIG is given as slow i.v. drip as a 3 - 4 % solution after testing for allergic reactions.

Cost : Rs. 1000 / g A course which requires 30 to 40 g i.v. will cost Rs. 40000 to 45000.

Platelet Transfusions

These are helpful in a dire emergency, especially if there is the risk of intracranial bleeding. Platelet transfusions are also useful adjuncts to

splenectomy if used as an intraoperative medication. Even in the absence of platelet transfusion, splenectomy can be undertaken, since the bleeding tendency is promptly arrested on clamping the splenic pedicle.

Immunosuppressants

Cyclophosphamide, azathioprine, and vincristine help to bring about remission in a resistant case.

Dose:	Cyclophosphamide oral	50-100 mg /day for 1 week or more
	Azathioprine	100mg/day(1-2mg/kg bw) for 1-2 weeks
	Vincristine	1-2 mg /day i.v. as a slow infusion, diluted in normal saline once a week. Total 1 or 2 doses

9.7.1.2 Chronic ITP

Corticosteroids in smaller doses: Prednisolone is started orally in dose of 0.5 - 1 mg/kg bw in order to achieve symptom relief, thereafter the smallest dose necessary to arrest bleeding is continued. If the daily requirement exceeds 5 - 10 mg of prednisolone, the patient is likely to develop adverse effects of steroids and therefore this is an indication to consider splenectomy. Corticosteroids may have to be continued indefinitely in many cases, with escalation of the dose during menstrual bleeding in women.

Indications for splenectomy in chronic ITP

1. Daily requirement of corticosteroids exceeds 10 - 15 mg.
2. Exacerbation during pregnancy.
3. When pregnancy is planned in a patient requiring 10 mg or more of prednisolone daily.

Contraindications of splenectomy

In children below 12 years splenectomy should be avoided if possible, due to the risk of pneumococcal infection. Vaccination against pneumococcus is mandatory in such cases.

Other drugs

Danazol

When the clinical improvement of both prednisolone and immunosuppressants is not satisfactory, danazol can be used as an add-on drug.

- I: This combines androgenic and anti-oestrogenic activity. It is used widely in gynaecological practice for endometriosis, menstrual disorders, gynaecomastia and others.
- C/I: Pregnancy, breast feeding, hepatic, renal or cardiac impairment, **androgen dependent tumours**.
- P/C: Epilepsy, migraine, cardiac, hepatic and renal dysfunction.

9. Drugs Acting on Blood and Blood Forming Organs

S/E: Nausea, headache, mild virilization.

P/A: Capsules 50 mg, 100 mg, 200 mg

Dose: When given in doses of 100 - 300 mg orally, it brings about clinical improvement in 50% of cases. The dose of corticosteroids can also be reduced.

D/I: Potentiates the action of oral anticoagulants. It inhibits the metabolism of carbamazepine and leads to increased plasma carbamazepine concentration.

Cost: Cap 50 mg (30) Rs. 215.00 - 240.00

9.7.1.3 Henoch schonle in purpura (vascular purpura)

This is not a haemorrhagic disorder. It is caused by allergic vasculitis. In most cases it is self-limiting. There is a tendency to recur on exposure to the allergen. Withdrawal of the causative factor and **prednisolone** in a dose of 0.25 to 0.5 mg/kg/bw bring about relief.

Antispasmodics such as **dicyclomine hydrochloride** 10- 20 mg thrice a day orally relieve abdominal pain. If renal involvement occurs, more active therapy is indicated.

There are several other forms of immunologically mediated vasculitis for which the main therapeutic modality is immunomodulation.

9.7.2 Thrombopathy

Occurrence of purpuric bleeding in the presence of normal or increased platelet count should suggest this possibility. Primary thrombocytopathies are rare, though they do occur at times. These respond to platelet transfusion which may be required to tide over bleeding episodes.

The vast majority of cases of platelet dysfunction is caused by drugs which are given for their specific antiplatelet action therapeutically in the prophylaxis and management of myocardial infarction, strokes and thromboembolism. eg. Aspirin, dipyridamole, ticlopidine.

Thrombocytopathy occurring as an unwanted side effect of other drugs

Mild thrombocytopathy may occur as a result of exposure to non-steroidal antiinflammatory drugs, betalactam antibiotics, and antihistamines. By themselves they seldom cause clinical bleeding, but in the presence of other underlying bleeding tendency, clinical bleeding may be precipitated. Withdrawal of the offending drug relieves the condition. The effect of aspirin lasts for upto 1 week after withdrawing the drug.

9.8 COAGULATION DEFECTS AND THEIR MANAGEMENT

9.8.1 Haemophilia and other Coagulopathies

These may be primary, as in the case of genetically transmitted disorders such as haemophilia A, (factor VIII deficiency) Christmas disease (syn-

haemophillia B factor IX deficiency) and deficiencies of one or more factors in the coagulation cascade. They vary in severity and haemorrhagic manifestation depending on the expressivity and penetrance of the genetic defect. Emergency treatment is to administer the deficient factor during the bleeding episodes. The coagulation factors are obtained by fractionation from whole plasma or by recombinant DNA technology. They are available in the freeze dried form.

Factor VIII (antihaemophilic globulin - AHG) is available as freeze-dried powder in vials of 2, 50, 500 and 1000 units. It is given as i.v. push doses or as a rapid i.v. drip, diluted in normal saline to run within 20 - 30 minutes. The aim is to raise the AHG levels in the patient as rapidly as possible to levels which arrest bleeding. The dose is calculated based on the weight of the patient and the level of the AHG in the plasma.

$$\text{Dose of AHG in units} = \frac{\text{percentage increase in factor desired} \times \text{weight in kg}}{2}$$

Factor IX : available as freeze dried powder for i.v. use in patients with haemophilia B

Factor VII a : recombinant factor VIIa is available for use in patients with the presence of inhibitors to factors VIII and IX.

Cost : AHG 1 unit Rs. 4.00.

Elective management

Initial diagnosis, assessment of severity and calculation of the appropriate dose of the coagulation factor have to be done in haematology centres equipped with full laboratory facilities. The general physician should take the follow-up management with close liaison with the haematologist.

Present day ideal treatment of haemophilia is to administer AHG prophylactically at regular intervals and at the earliest evidence of bleeding. The patient and his family members are instructed to administer AHG even before reaching the hospital. The aim is to prevent the occurrence of haemorrhagic episodes which lead to progressive destruction of joints and other crippling deformities.

The world haemophilia federation which assists patients and doctors who are interested in haemophilia has several branches in India, including a few in Kerala.

9.8.2 Fibrinogen deficiency

Rarely this may be congenital. More often it is the result of consumption coagulopathy resulting in defibrination syndrome. In primary fibrinogen deficiency, fibrinogen can be given.

S/E : anaphylactic reactions.

In disseminated intravascular coagulation secondary fibrinolysis occurs, which is a protective phenomenon. Infusion of fibrinogen without

9. Drugs Acting on Blood and Blood Forming Organs

arresting the primary process is of no avail.

9.9 ANTIPLATELET DRUGS

Several drugs are used to inhibit the procoagulant activities of the platelets. Different drugs act by inhibiting different process of the platelets. Antiplatelet drugs are used widely for the prophylaxis and the management of several thrombotic and embolic diseases such as coronary vascular disease, cerebral thrombosis, peripheral vascular occlusion and venous thrombosis. The common drugs in this group include aspirin, dipyridamole and ticlopidine. More specific antiplatelet drugs are available for specific purposes such as prevention of thrombosis of intracoronary stents. eg. Abciximab which is a monoclonal antibody against platelet receptors.

Therapeutic doses of antiplatelet drugs and their adverse side effects

Drug	Daily Dose	Route of administration	Side effects
Aspirin	75 - 150 mg	oral, soon after food	gastritis, pain and bleeding from stomach, mild generalised bleeding tendency
Dipyridamole	300 - 600 mg	oral b.d. or t.d.s.	gastrointestinal disturbances, nausea and vomiting, headache
Ticlopidine	250 - 500 mg	oral tablets b.d.	nausea and vomiting, anorexia, agranulocytosis

9.10 ANTICOAGULANTS

These inhibit the coagulation pathway in one or other step thereby preventing thrombus formation. They are indicated in the prevention and treatment of thromboembolic disease.

- 1: Recurrent venous thromboembolism, ischaemic heart disease - myocardial infarction, cerebral venous thrombosis, prevention of thromboembolism in arterial fibrillation, implantation of prosthetic heart valves, arterial conduits, recurrent pulmonary embolism, as a follow up therapy after the use of thrombolytic agents such as tissue plasminogen activator.

Available drugs

1. Heparin and it's derivatives which are given parenterally.
2. Oral anticoagulant drugs coumarins and indanediones.

9.10.1 Heparin

Heparin is present naturally in mast cells and the liver, but in health there is no free heparin detectable in plasma. Commercially available heparin is produced from animal lungs. Standard heparin (SH) is a mixture of compounds with molecular weights ranging from 2000 - 20000 (mean 5000) and their anticoagulant activity is also variable. By physico-chemical methods low molecular weight heparin (LMWH) having molecular weights ranging from 2000 - 10000 is produced. eg. Dalteparin sodium.

SH and LMWH show difference in their actions and chemical effects.

Action

Heparin inhibits coagulation both in vitro and in vivo. SH acts mainly through the medium antithrombin III (AT III) which acts as cofactor. AT III is part of the natural defence mechanism of the body against thrombosis. The major ultimate actions of heparin are to inhibit the formation of thrombin from prothrombin and aggregation of platelets caused by thrombin. Heparin produces a conformational change in AT III. This accelerates and augments the effects AT III against thrombin and factor Xa about 1000 folds. SH binds to plasma proteins and platelets in varying degrees and therefore its action is less consistent when compared to LMWH which has more bioavailability. LMWH acts more as anti-factor Xa and this effect is 2-4 times that of SH. Though LMWH is more expensive than SH its advantage in special situations makes it the drug of choice in cardiovascular and neurovascular indications.

- I: 1. As prophylactic and curative in venous and arterial thrombo-embolic disease. The anticoagulant effect is rapidly achieved by parenteral administration of heparin. Simultaneously oral anticoagulants are also started. The latter takes 2-3 days for their effect to be established. By this time the heparin is withdrawn and anticoagulation is continued for prolonged periods depending on the indication.
2. Disseminated intravascular coagulation: heparin inhibits the widespread intramuscular thrombotic process and thus arrests the further vicious circle from developing.

S/E: Bleeding from the gastrointestinal and urinary tracts, intracranial bleeding, thrombocytopenia and purpuric bleeding, allergic manifestations, alopecia, osteoporosis on prolonged administration.

P/A: Vial 5000 - 25000 units (1000 units / mL to 5000 units / mL)
1 mg is approximately 100 units.

Dose: (1) 5000 - 10000 units every hour or as i.v. infusion 20000 units, diluted in 5% glucose solution or normal saline, run over 12 - 24 hrs. The dose and rate of administration depends on the indications and degree of anticoagulation desired.

- (2) Repeated deep i.m. or subadipose injections 2000 - 10000 units repeated 6 h.

9. Drugs Acting on Blood and Blood Forming Organs

The dose is titrated by keeping the clotting time 2-3 times the normal. A more reliable parameter is the activated partial thromboplastin time (APTT) which should be maintained at 1 1/2 - 2 times the normal.

Dose for small adults and children

15-25 units/kg bw /h i.v. infusion continuously or 250 units/kg bw every 12 h by s.c. injection.

In general the doses required to prevent venous thrombosis are considerably less in comparison to those required for arterial thromboembolism (2000 units once or twice a day V/s 5000 - 10000 units 6 h).

Low molecular weight heparin

Note : LMWH has distinct advantages over SH. These are :

1. *Smaller dose and longer duration of action.*
2. *Once or twice a day administration.*
3. *More consistent clinical effects.*
4. *Absence of thrombocytopenia.*
5. *No need to have regular laboratory monitoring when given in the usual dosage.*
6. *Can be given as outpatient therapy and at home.*

P/A : Solution containing 2500 iu/mL - 4 mL ampoules.

Dose : 2000 - 5000 units given s.c. once or twice a day.

ANTIDOTE TO HEPARIN

Protamine sulphate

S/E : Flushing, hypotension, bradycardia and dyspnoea.

P/A : 5 mL ampoules, 10 mg/mL.

Dose : Protamine sulphate 1% solution given i.v. neutralizes heparin and rapidly reverses its effect. 1 mg protamine sulphate for 100 units (1 mg) of heparin given as the last dose. If given after 3-4 h of the last dose of heparin, only smaller amounts of protamine are needed. It is effective in neutralizing dalteparin as well.

9.10.2 Oral anticoagulants

The two classes of drugs in this groups are the coumarins and indanediones. They are effective when given orally, but they do not possess any anticoagulant activity in vitro.

Mode of action

They prevent the activation of vitamin K - dependent coagulation factors ie., VII, IX and X in the liver. When given orally they are well absorbed and

peak serum levels are obtained in 2 - 3 hrs. They are concentrated in the liver which is their main site of action. Their action is slow, taking 2 - 3 days for maximal effect, but once established, the anticoagulant effect persists for 4 - 7 days even after withdrawal of the drug.

Coumarin groups of drugs

Warfarin sodium

When given orally it is absorbed rapidly. Its half life is 15 - 70 hours.

P/A: Tablets 1 mg, 3 mg, 5 mg, 10 mg and 20 mg.

Parenteral preparations for i.m. and i.v. use is available but it is seldom used. Therapy is started with a loading dose of 30 - 50 mg daily along with heparin. The dose is tapered off daily to 10 mg and thereafter 3 - 5 mg/day in order to maintain the prothrombin time as 2 to 3.5 times the control value, or international normalized ration (INR) as 2 - 3 depending upon the underlying indication.

Indanediones

Phenindione

This is an effective anticoagulant. When given orally it is rapidly absorbed. Its half life is 5-10 h.

C/I: Pregnancy, lactation.

S/E: Hemorrhagic manifestations - gastrointestinal, urinary and intracranial.

P/A: Tablets 10 mg, 25 mg and 50 mg.

Dose: The initial loading dose is 200 - 300 mg / day. It is rapidly tapered off daily to 100 mg and later to 50 mg daily. The maintenance dose is around 50 mg in order to maintain optimal anticoagulation.

D/I: Oral anticoagulants produce several important drug interactions which lead either to enhancement or blunting of their effects.

9.10.2.1 Drugs which enhance anticoagulant effects

1. Sulpha drugs, clofibrate, ethacrynic acid, nalidixic acid.

The anticoagulant is displaced by the following drugs from its plasma protein binding sites and therefore the anticoagulant activity is enhanced.

2. Further depression of Vit.K related clotting factors by quinine, quinidine, thyroxine.
3. Anabolic steroids impairment of hepatic function.

9.10.2.2 Drugs which impair the anticoagulant action

Genetic variation leads to microsomal induction in the liver and rapid destruction of the anticoagulant. Barbiturates, phenytoin, haloperidol,

9. Drugs Acting on Blood and Blood Forming Organs

griseofulvin, rifampicin will cause microsomal enzyme induction in the liver and rapid destruction of the anticoagulant.

Since oral anticoagulants are administered over long periods for prophylaxis and treatment of life threatening conditions, it is important to elicit drug history which should suggest drug interactions.

9.10.2.3 Antidote to oral anticoagulants

The first step is to withdraw the anticoagulant. If the prothrombin time is only 3 times the normal this measure is enough. If the PTT is further prolonged, phytomenadion (Vitamin K₁) 5 mg given by slow i.v. injection corrects the haemorrhagic tendency within a few hours. If the condition is life threatening or the hepatic function is unsatisfactory, concentrates of factors II, IX, X and VII have to be given. If the concentrates are not available, fresh frozen plasma is infused, approximately one litre for an adult.

9.11 ANTIFIBRINOLYTIC DRUGS

These are indicated in primary fibrinolytic states with clinical haemorrhagic tendency and in the rare event of haemorrhagic complications caused by thrombolytic agents.

The drugs include the synthetic aminoacids epsilon aminocaproic acid (EACA) and tranexamic acid and the polypeptide aprotinin. All of these inhibit the conversion of plasminogen to plasmin and further action of plasmin. They also inhibit the action of thrombolytic agents like streptokinase and urokinase. They can be used with caution as follow-up therapy in DIC after controlling the primary process.

Epsilon amino caproic acid (EACA)

P/A: Tablets 0.5 g, 1 g.

Dose: 3-4 g, given t.d.s or q.d.s. to a total of 20-25 g/day. It is rapidly absorbed and a single dose gives satisfactory blood levels for 4 hrs.

Parenteral dose: 5 - 10 g by i.v. injection in the first hour followed by 2 g every hour for the next 2 - 3 hrs, this is followed up with oral tablets 4 g 4 h. The total daily dose should not exceed 30 g.

EACA is excreted rapidly in urine and the urinary concentration exceeds the blood level. Therefore in bleeding from the urinary tract only smaller doses are required. It is used to arrest bleeding in prostatic surgery and after dental extractions.

Tranexamic acid

P/A: Scored tablets of 500 mg

Dose: Oral: 15 - 25 mg/kg b.d. or t.d.s.

Parenteral: Slow i.v. injection in a dose of 0.5 - 1 g t.d.s.

Aprotinin

I: This inhibits the action of plasmin and kallikrein, thereby preventing fibrinolysis. It is used as an intraoperative infusion during major surgery such as open heart surgery in order to prevent excessive blood loss.

Dose: 5,00,000 to 10,00,000 units given over 10 minutes, repeated hourly in doses of 2,00,000 units till the bleeding is arrested. Aprotinin also inhibits the action of pancreatic trypsin and therefore it is used in acute pancreatitis.

9.12 THROMBOLYTIC AGENTS

Recanalisation of arteries and veins occluded by recent thrombi is achieved by the use of fibrinolytic drugs systemically or in special circumstances delivered at the local site through special catheters. In myocardial infarction (MI) use of these drugs at the earliest opportunity during the evolution of the disease has served to limit infarct size, prevent death in the acute phase and reduce the incidence of longterm myocardial dysfunction and fatal arrhythmias. So it is absolutely necessary that all practicing physicians should be fully conversant with the use of thrombolytic agents in all aspects. Often it is the physician of first contact - either the family physician or the internist who has to take the decision for immediate thrombolysis in MI.

Indication for thrombolysis

Presence of acute MI, characterised by chest pain and atleast ST elevation in the ECG.

Place where thrombolysis is administered : Even though the ideal is to give the thrombolytic agents in the hospital environment, in view of the fact that earlier the thrombolysis is achieved, better is the result, these drugs may have to be given at home before transit to hospital or in the ambulance.

Drugs :

The freely available drugs are streptokinase and urokinase. Several other drugs such as tissueplasminogen activator (tPA) and it's derivatives are available for use in special situations in intensive coronary care units.

Streptokinase (SK)

Thrombolytic therapy

I: Acute myocardial infarction, pulmonary embolism, peripheral arterial thrombosis and thrombosis of arteriovenous shunts, cerebral thrombosis - with caution.

C/I: Recent surgery, cerebrovascular accidents, haemorrhagic diathesis. Diabetes mellitus is not a contra indication for thrombolysis.

9. Drugs Acting on Blood and Blood Forming Organs

P/C : Use puncture sites (arterial and venous) which are compressible. efficacy of this drug is less after recent streptococcal infections. Do not repeat in MI occurring 1 week - 1 year after administration due to the fear of sensitization.

S/E : Bleeding from sites of recent surgery, or trauma, ulcers and wounds. Intracranial bleeding may occur.

P/A : Available as injections 2,50,000 iu, 7,50,000 iu, 15,00,000 iu

Dose : SK is given i.v. over 30 minutes initially and if necessary 1,00,000 to 1,50,000 units repeated at 1 hour and 2 hrs by i.v. push doses. The initial injection has to be slow, in order to avoid hypotension. Effective recanalisation of the coronary artery is evidenced by relief of anginal pain and recovery of the ECG abnormality.

D/I : Use with caution in patients already receiving anticoagulants like heparin.

Cost : Inj vial (1500000 iu) about Rs. 3500.00

Urokinase

I:, C/I:, S/E : Same as streptokinase

P/C : Bleeding from puncture sites.

P/A : Available as injections 50,000 iu, 2,50,000 iu, 5,00,000 iu, 7,50,000 iu, 10,00,000 iu.

Dose : Administration is similar to that of streptokinase but the injection can be given i.v. within 10 min. 3,00,000 units or 4,400 units/kg/bw. Unlike streptokinase urokinase produces less of allergic reactions. If the condition is resistant to streptokinase, urokinase can still be effective. The latter is more expensive.

D/I : Aspirin and indomethacin can cause haemorrhage. Heparin and oral anticoagulants will increase the risk of bleeding.

Cost : Inj vial (500000 iu) Rs. 3700.00

Antidote in case of overdose : antifibrinolytic drugs

eg. EACA, or tranexamic acid in doses of 4 -5 g oral 6 h or 15 - 25 mg/kg bw orally t.d.s. respectively.

Other drugs include tPA (Tissue Plasminogen Activator) (Altepase), rTPA and its derivatives. These are all used for highly specialised cardiac neurological surgical work.

CHAPTER 10 : DRUGS USED IN NEUROLOGICAL DISORDERS

10.1. DRUGS WHICH ENHANCE NEUROMUSCULAR TRANSMISSION

These drugs are mainly used for the treatment of myasthenia gravis. The basic abnormality of myasthenia gravis is that it is an autoimmune disease resulting in a reduction of available acetylcholine receptors at the neuromuscular junction leading to impairment of neuromuscular transmission and subsequent weakness. Anticholinesterases are used as first-line treatment in myasthenia gravis. Corticosteroids are only given concomitantly if anticholinesterase treatment is failing. Plasmapheresis may produce temporary remission in otherwise unresponsive patients.

10.1.1 Anticholinesterases

Anticholinesterase drugs enhance neuromuscular transmission in voluntary and involuntary muscle in myasthenia gravis. They prolong the action of acetylcholine by inhibiting the action of the enzyme cholinesterase

Neostigmine ☆

- I: Myasthenia gravis, reversal of non-depolarising neuromuscular blockade.
- C/I: Intestinal or urinary obstruction.
- P/C: Asthma, recent myocardial infarction, epilepsy, hypotension, parkinsonism, peptic ulceration, renal impairment, pregnancy and breast-feeding.
- S/E: Nausea, vomiting, diarrhoea, and abdominal cramps. Signs of overdose are increased gastro-intestinal motility, bronchial secretions, and sweating, involuntary defecation and micturition, miosis, hypotension, and weakness leading to fasciculation and paralysis.
- P/A: Tablet 15 mg,
Injection 0.5mg/mL.
- Dose: Oral : neostigmine bromide 15-30 mg at regular intervals throughout day, total daily dose 75-300 mg
Neonate 1-5 mg every 4 hours, half an hour before feeds.
For children : up to 6 years initially 7.5 mg.
6-12 years initially 15 mg, usual total daily dose 15-90 mg.
Parenteral: By s.c. or i.m., neostigmine methylsulphate 1-2.5 mg at

10. Drugs used in Neurological Disorders

suitable intervals as required (usual daily dose 5-20 mg).

Neonate 50-250 mcg every 4 hrs half an hour before feeds.

For children 200-500 mcg as required.

D/I: Quinidine, chloroquine, propranolol, lithium, amino glycosides, clindamycin, lincomycin and polymyxins antagonises effect of neostigmine and pyridostigmine.

Cost : Tab 15 mg (10) Rs. 45.00- 46.00

Inj 0.5 mg/mL (10 x 1 mL) Rs. 39.00- 40.00

Pyridostigmine Bromide

I: Myasthenia gravis.

C/I, P/C, S/E: Same as for neostigmine; weaker muscarinic action.

P/A: Tablet 60 mg

Injection

Syrup

Dose: Oral 30-120 mg at regular intervals as required, total daily dose 0.3-1.2 g; neonate 5-10 mg every 4 h, 1/2 - 1 hr before feeds;

For children upto 6 years initially 30 mg,

6-12 years initially 60 mg, usual total daily dose 30-360 mg.

D/I: Same as neostigmine.

Cost : Tab 60mg (150) Rs. 600.00

Other preparations are not freely available.

Edrophonium Chloride

I: Has a very brief action and is used mainly for the diagnosis of myasthenia gravis. It is also used to determine whether a patient with myasthenia is receiving inadequate or excessive treatment with cholinergic drugs; surgery.

C/I, P/C, S/E, D/I: Same as neostigmine.

P/A: Injection 10 mg/mL (1 mL ampoule)

Dose: Diagnosis of myasthenia gravis, i.v. 2 mg followed after 30 second by 8 mg.

Detection of overdose or underdosage of cholinergic drugs, i.v., 2mg.

For children i.v., 20 mcg/kg followed after 30 seconds by 80 mcg/kg

Cost : Not commercially available.

10.1.2 Skeletal Muscle Relaxants

These drugs are used for the relief of chronic muscle spasm or spasticity; they are not indicated for spasm associated with minor injuries. They act

principally on the central nervous system with the exception of dantrolene, which has a peripheral site of action. They differ in their action from the muscle relaxants used in anesthesia, (which block transmission at the neuromuscular junction)

Baclofen

I: Chronic severe spasticity resulting from disorders such as multiple sclerosis or traumatic partial injury to spinal cord.

C/I: Peptic ulceration.

P/C: Psychiatric illness, cerebrovascular disease, diabetes mellitus; respiratory, hepatic or renal impairment; epilepsy; history of peptic ulcer; pregnancy; porphyria.

S/E: Sedation, drowsiness, nausea, confusion, ataxia, hallucination, insomnia, convulsion, respiratory and cardiovascular depression, hypotension.

P/A: Tablet 10mg and 25 mg.

Dose: Oral : 5 mg t.d.s., preferably after food, gradually increased; maximum 100 mg daily;

For children over 10 years 0.75-2mg/kg daily, maximum 2.5 mg/kg daily, or 2.5 mg q.d.s increased gradually according to age to the effective maintenance dose:

1-2 years 10-20 mg daily,

2-6 years 20-30 mg daily,

6-10 years 30-60 mg daily.

D/I: Mutual potentiation with CNS depressants and alcohol. Concomitant use with levodopa in parkinson's patients may result in confusion, agitation, hallucinations. When given concurrently with antihypertensive drug the hypotensive effect may be aggravated.

Cost : Tab 10 mg(10) Rs. 60.00 – 62.00.

Diazepam ☆

I: Muscle spasm of varied aetiology, including tetanus.

Dose: Oral : 2-15 mg daily in divided doses, increased if necessary in spastic conditions to 60 mg daily according to response by i.m. or by slow i.v. in acute muscle spasm, 10 mg repeated if necessary after 4 hrs. Parenteral : Tetanus adult and child by i.v., 100 - 300 mcg / kg repeated every 1 - 4 h; by i.v. infusion (or by nasoduodenal tube 3-10mg/kg over 24 hrs, adjusted according to response.

10.1.3 Other Muscle Relaxants

The clinical efficacy of carisoprodol, meprobamate, and methocarbamol

10. Drugs used in Neurological Disorders

as muscle relaxants is not well established although they have been included in compound analgesic preparations.

Carisoprodol

I: Short-term symptomatic relief of muscle spasm

C/I: Acute pulmonary insufficiency; porphyria

P/C: Respiratory disease, muscle weakness, epilepsy, pregnancy

S/E: Drowsiness, gastrointestinal disturbances, hypotension.

P/A: Tablet 350 mg.

Dose: 350 mg t.d.s.

D/I: Additive actions with concurrent use of alcohol, other CNS depressants or psychotropic drugs.

Cost : Tab 350 mg (10) Rs. 28.00 – 30.00

Methocarbamol

I: Short term symptomatic relief of muscle spasm.

C/I: Coma, brain damage, epilepsy, and myasthenia gravis

P/C: Hepatic and renal impairment.

S/E: Lassitude, confusion, allergic rash and convulsions.

P/A: Tablet 500 mg,

Injection 100mg/10 mL.

Dose: Oral : 1.5 g q.d.s. may be reduced to 750 mg t.d.s.

Parenteral : slow i.v. infusion, 1-3 g (maximum rate 300mg/min, maximum dose 3 g daily for 3 days.

D/I: CNS depressant effects is potentiated with alcohol and other CNS depressant drugs, efficacy of anoretics and anticholinergics increased.

Cost : Inj 100 mg (10 mL) Rs. 12.00 – 13.00

Tab 500 mg (10) Rs. 23.00 – 24.00

10.2 ANTIEPILEPTICS

The object of treatment of epilepsy is to prevent the occurrence of seizures. An effective plasma concentration of the drug has to be maintained by careful adjustment of dosage, starting with low doses and increasing gradually until seizures are controlled or toxic effects occur.

The frequency of administration : should be kept as low as possible to encourage better patient compliance. Young children metabolise antiepileptics more rapidly than adults and therefore may require more frequent and relatively higher doses.

Combination Therapy : Therapy with several antiepileptics drugs concurrently should generally be avoided. Monotherapy is to be preferred. A second drug should be given only if seizures continue even after giving the

maximum tolerated dose. Another disadvantage of multiple therapy is that drug interactions occur between various antiepileptics.

Withdrawal : Abrupt withdrawal of antiepileptics, particularly barbiturates and benzodiazepines, should be avoided as this may precipitate severe rebound seizures. Reduction in dosage should be carried out in stages and in the case of barbiturates, the withdrawal process may take several months. The change over from one antiepileptics regimen to another should be made cautiously, withdrawing the first drug only when the new drug has taken its effect.

Administration during pregnancy increases the risk of teratogenicity which is less if the treatment is limited to a single drug. Women on antiepileptic drugs who become pregnant should be counselled and offered antenatal screening which should include estimation of alpha-fetoprotein and a second trimester ultrasound scan.

The risk of neural tube defects can be reduced by supplementing 400 mcg to 1 mg of folate daily. In those receiving antiepileptics such as carbamazepine and phenytoin dose of folic acid may have to be increased up to 5 mg/day

Breast-feeding is permissible for women taking ordinary doses of antiepileptic drugs except barbiturates and ethosuximide.

Carbamazepine ☆

Carbamazepine is the drug of choice for simple and complex partial seizures and for tonic-clonic seizures regardless of whether they are primary or secondary to a focal discharge. It has a wider therapeutic index than phenytoin and the relationship between dose and plasma concentration is linear. Monitoring plasma concentrations may be helpful in determining optimum dosage. The optimum blood levels are 4–12 mg/L (20–50 micromol/L). It has fewer side effects than phenytoin or barbiturates. Reversible blurring of vision, dizziness and unsteadiness are dose-related and they warrant reduction of dosage. Altering the timing of medication may reduce these side-effects; use of modified release tablets also significantly lessens the incidence of dose-related side effects. It is essential to initiate carbamazepine therapy at a dosage of 100–200 mg daily and build this up slowly with increments of 100–200 mg every two weeks.

I: All forms of epilepsy except absence seizures.

Trigeminal neuralgia

Prophylaxis in manic-depressive illness.

C/I: Atrioventricular conduction abnormalities, history of bone marrow depression and porphyria.

P/C: Avoid sudden withdrawal. Patients or their carers should be told how to recognize signs of blood, liver or skin disorders, and advised to seek immediate medical attention if symptoms such as fever,

10. Drugs used in Neurological Disorders

sore throat, rash, mouth ulcers, bruising or bleeding develop. Leucopenia which is severe, progressive, or associated with clinical symptoms, requires withdrawal of the drug.

S/E: Nausea and vomiting, dizziness, drowsiness, headache, ataxia, confusion and agitation visual disturbances (especially double vision), constipation or diarrhoea, anorexia; mild transient generalized erythematous rash, leucopenia and other blood disorders including thrombocytopenia, agranulocytosis and aplastic anaemia. Other side-effects include cholestatic jaundice, hepatitis and acute renal failure, Stevens-Johnson syndrome, toxic epidermal necrolysis, alopecia, thromboembolism, arthralgia, fever, lymphnode enlargement, cardiac conduction disturbances, dyskinesias, paraesthesia, depression, impotence and impaired fertility, gynecomastia, galactorrhoea, aggression, psychosis, photosensitivity, allergic pneumonitis and oedema.

P/A: Tablet 100 mg, 200 mg, 400 mg,

Syrup 100 mg/5mL

Dose: Epilepsy

Oral : Adult : initially 100-200 mg o.d. to b.d., increased slowly to the usual dose of 800-1200 mg daily in divided doses. In some cases 1600-2000 mg daily may be needed; in elderly reduce initial dose. Children daily in divided doses, up to one year 100-200 mg,

1-5 years 200-400 mg,

5-10 years 400-600 mg,

10-15 years 600-1000 mg.

D/I: Calcium channel blockers, dextropropoxyphene, erythromycin, isoniazid enhances effect of carbamazepine. Metabolism of doxycycline, clonazepam accelerated (reduced effect). Reduced anticoagulant effect of nicoumalone and warfarin. Antidepressants and antipsychotics will antagonise the anticonvulsant effect. Enhanced toxicity with other antiepileptics.

Note: Plasma concentration for optimum response 4-12 mg/L (20-50 micromol/L).

Cost: Tab 200mg (10) Rs 18.00 -20.00

Syrup 100mg/5 mL (50mL) Rs 18.00-20.00

Ethosuximide

I: Drug of choice in simple absence seizures; it may also be used in myoclonic seizures and in atypical absence, atonic, and tonic seizures.

C/I: Hypersensitivity

P/C: Same as for carbamazepine. In addition pregnancy and breast feeding are special contraindications.

S/E: Gastrointestinal disturbances, weight loss, drowsiness, dizziness, ataxia, dyskinesia, hiccup, photophobia, headache, depression, and mild euphoria. Psychotic states, rashes, hepatic and renal changes and haematological disorders such as agranulocytosis and aplastic anaemia occur rarely. Systemic lupus erythematosus and erythema multiforme may occur. Other side effects include gum hypertrophy, swelling of tongue, irritability, hyperactivity, sleep disturbances, night terrors, inability to concentrate, aggressiveness, increased libido, myopia and vaginal bleeding.

P/A: Syrup 250 mg/5mL

Dose: Adult and Child over 6 years : start initially with 500 mg daily, increased by 250 mg at intervals of 4-7 days to the usual dose of 1-1.5 g daily. Occasionally up to 2 g daily may be needed.

Children upto 6 years : initially 250 mg daily, increased gradually to usual dose of 20mg/kg day. If the daily dose exceeds 150 mg in adults and 750 mg in children extra caution is required.

D/I: Isoniazid increases plasma concentrations, increases the risk of toxicity. With antidepressants and antipsychotics antagonism of effect. Enhanced toxicity with other antiepileptics.

Note: Plasma concentration for optimum response 40-100 mg/L (300-700 micromol/L)

Cost : Syrup 50 mg /mL (114 mL) Rs. 39.00 – 40.00

Phenobarbitone ☆

I: All forms of epilepsy and status epilepticus except absence seizures.

C/I: Hypersensitivity, acute intermittent porphyria, severe renal and hepatic disorders and severe myocardial damage.

P/C: Elderly, debilitated, children, impaired renal or hepatic function, respiratory depression, breast feeding, avoid sudden withdrawal.

S/E: Drowsiness, lethargy, mental depression, ataxia and allergic skin reactions; paradoxical excitement, restlessness and confusion in the elderly and hyperkinesia in children; megaloblastic anaemia.

P/A: Tablets 30mg, 60mg.

Injection 200 mg/mL

Dose: Oral : Adult - 60 to 180 mg at night.

Children - 5 to 8 mg/kg daily

Parenteral : i.m. or i.v. 50-200 mg, repeated every 6 hrs if necessary; maximum 600 mg daily. Dilute injection 1 in 10 with water before intravenous administration for status epilepticus.

D/I: Reduced effect of antiarrhythmics, theophylline, cyclosporine, antibacterials and anticoagulants. Antagonism of anticonvulsant effect with anti-depressants and oral contraceptives.

10. Drugs used in Neurological Disorders

Note: For therapeutic purposes phenobarbitone and phenobarbitone sodium may be considered equivalent in effect. Plasma concentration for optimum response 15-40 mcg/L (60-180 micromol/L)

Cost :	Tab 30 mg	(10)	Rs. 4.00 – 6.00
	Inj 200 mg/mL	(10 x 1 mL)	Rs. 125.00 – 126.00

Primidone

I: All forms of epilepsy except absence seizure, essential tremor

C/I: Same as for phenobarbitone.

P, C:& S, E: Same as for phenobarbitone. Drowsiness, ataxia, nausea, visual disturbances, and rashes may occur initially but may subside on continued administration..

P/A: Tablets 250 mg

Dose: Epilepsy: initially, 125 mg daily h.s. increased by 125 mg every 3 days to 500 mg daily in 2 divided doses then increased by 250 mg every 3 days to a maximum of 1.5 g daily in divided doses.

Children below 2 years - upto 500 mg

2 – 5 years - upto 750 mg

6 – 9 years – upto 1 g.

Note: Monitor plasma concentrations of derived phenobarbitone. Optimum range as for phenobarbitone.

D/I: Same as phenobarbitone

Cost : Tab 250 mg (10) Rs. 23.00 – 24.00

Phenytoin ☆

I: All forms of epilepsy especially tonic-clonic and partial seizure except absence seizure, trigeminal neuralgia.

C/I: A.V. block, acute intermittant porphyria

P/C: Phenytoin should not be given i.m and it should not be added to i.v. infusion along with other drugs. Impaired liver function pregnancy and lactation

S/E: Nausea, vomiting, mental confusion, dizziness, headache, tremor, transient nervousness and insomnia occur commonly; rarely dyskinesias, peripheral neuropathy; ataxia, slurred speech, nystagmus and blurred vision are signs of overdose; rashes, coarse facies, acne, hirsutism, fever and hepatitis; lupus erythematosus, erythema multiforme (Stevens-Johnson Syndrome), toxic epidermal necrolysis, polyarteritis nodosa; lymphadenopathy; gingival hypertrophy and tenderness; rarely hematological effects including megaloblastic anaemia (may be treated with folic acid), leucopenia, thrombocytopenia, agranulocytosis, and aplastic anaemia; plasma calcium may be lowered (rickets and osteomalacia).

P/A: Tablet 50 mg and 100 mg

Capsule 100 mg,

Suspension 25 mg/mL,

Injection 50 mg/mL.

Dose: Oral: Adult-initially 3-4 mg/kg daily or 150-300 mg daily as a single dose or in two divided doses increased gradually as necessary. The usual dose 300-400 mg daily upto a maximum 600 mg daily;

Children: 5 to 8 mg/kg daily in 1 or 2 doses taken preferably with or after food.

Parenteral: Adult-slow i.v. or infusion in status epilepticus, with blood pressure and ECG monitoring in a dose of 15 mg/kg at a rate not exceeding 50 mg per minute, as the loading dose. Maintenance doses of about 100 mg should be given thereafter at intervals of about 100 mg should be given thereafter at intervals of 6 - 8 hrs, monitored by measurement of plasma concentrations; rate and dose reduced according to weight.

Children - 15 mg/kg as a loading dose (neonate 15-20 mg /kg at rate of 1-3 mg/kg/min).

D/I: Increased effect of phenytoin with analgesics. Amiodarone increases plasma phenytoin concentration. Phenytoin reduces plasma concentration of disopyramide, mexiletine and quinidine. Food interferes with absorption of phenytoin. Effect of isradipine reduced. Reduced effect of digitoxin. Plasma phenytoin concentration occasionally reduced by folic acid. Plasma concentration for optimum response 10-20 mg/L (40-80 micromol /L).

Note: For i.v. infusion, use freshly prepared solution in half normal saline.

Cost: Tab 50 mg	(100)	Rs 25.00-29.00
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Inj 50mg	2 mL	Rs 5.00- 6.00
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Sodium valproate ☆

I: All forms of epilepsy. It is effective in controlling tonic-clonic seizures, particularly in primary generalised epilepsy. It is a drug of choice in primary generalised epilepsy, generalised absences and myoclonic seizures, and may be tried in atypical absence, atonic, and tonic seizures. It has probably similar efficacy to that of carbamazepine and phenytoin. Plasma concentrations do not always correlate with clinical efficacy and therefore, routine monitoring is not required. The drug has widespread metabolic effects and may have dose-related side effects.

C/I: Active liver disease, family history of severe hepatic dysfunction

P/C: Monitor liver function before therapy and during the first 6 months

10. Drugs used in Neurological Disorders

especially in patients at higher risk. In patients receiving this drug exclude bleeding tendency before major surgery, severe renal impairment; pregnancy, breast-feeding, systemic lupus erythematosus, acute porphyria. False positive urine tests for ketosis may occur. Avoid sudden withdrawal. There is increased risk of neural tube defects and neonatal bleeding and neonatal hepatotoxicity if the drug is given during pregnancy. Liver dysfunction including fatal hepatic failure has occurred in association with valproate (especially in children under 3 years of age).

S/E: Gastric irritation, nausea, ataxia and tremor, increased appetite and weight gain, transient hairloss, oedema, thrombocytopenia and inhibition of platelet aggregation, impaired hepatic function leading rarely to fatal hepatic failure, rashes, sedation, rarely pancreatitis, leucopenia, red cell hypoplasia, fibrinogen reduction, irregular periods, amenorrhoea and gynaecomastia.

P/A: Tablet 200 mg and 500 mg
Syrup 200 mg/5mL

Dose: Adult - initially, 600 mg daily given in 2 divided doses, preferably after food, increased by 200 mg/day at 3 day intervals to a maximum of 2.5 g daily in divided doses. Usual maintenance is 1-2 g daily (20-30 mg/kg bw daily).

Children Upto 20 kg : 20mg/kg bw daily in divided doses. This may be increased depending on the response. If doses above 40 mg/kg daily are given it is preferable to monitor plasma levels.

Over 20 kg : initially 400 mg daily in divided doses increased until control. Usually 20-30mg/kg bw daily may be required upto a maximum of 35 mg/kg daily.

D/I: Enhanced effect by aspirin. With antidepressants and antipsychotics, antagonism of anticonvulsant effect. Enhanced toxic effects with other antiepileptics

Cost : Tab 200 mg	(10)	Rs. 15.00 – 20.00
Syrup 200 mg/5 mL	(100 mL)	Rs. 45.00 – 60.00

Vigabatrin

I: Is a newer antiepileptic which acts by inhibition of GABA transaminase. Trials have shown that it is effective in many patients with refractory epilepsy, especially partial seizures with or without generalization. Well absorbed orally, excreted unchanged in urine. Partial epilepsy in mentally retarded patients

C/I: Pregnancy and breast feeding

P/C: Renal impairment, closely monitor neurological functions, avoid sudden withdrawal.

S/E: Mild, drowsiness, mental confusion, amnesia, behavioural changes and agitation in children.

P/A: Tablet 500mg

Dose: With current antiepileptic therapy, initially 1 g daily in single or 2 divided doses, then increased according to response in steps of 500 mg; usual range 2-4 g daily.

Children initially 40mg/kg daily increased according to response to 80-100 mg/kg daily.

For infantile spasms (West's syndrome) monotherapy, 60-100 mg/kg daily, adjusted according to response over 7 days, maximum of 150 mg/kg daily may be given..

D/I: Causes a 20% decrease in plasma phenytoin concentration.

Cost : Not freely available.

Clonazepam

I: It is a benzodiazepine with prominent anticonvulsant properties. Clonazepam has been primarily used in petitmal . It is also used as an adjuvant in myoclonic and akinetic epilepsy and may afford some benefit in infantile spasms.

C/I: Respiratory depression, acute pulmonary insufficiency, porphyria.

P/C: Respiratory disease, hepatic and renal impairment, elderly and debilitated, pregnancy and breast feeding .

S/E: Sedation, dullness, behavioural abnormalities in children, drowsiness, fatigue, dizziness, muscle hypotonia, coordination disturbances, hypersalivation in infants, blood disorders

P/A: Tablets 0.5 mg, 2 mg.

Dose: Adult - 1 mg (elderly 500 mcg), initially at night for 4 night, increased over 2-4 weeks to a usual maintenance dose of 4-8 mg daily in divided dose;

Children up to 1 year - 250 mcg increased as above to 0.5-1 mg,

1-5 years - 250 mcg increased to 1-3 mg,

5-12 years - 500 mcg increased to 3-6 mg.

D/I: Metabolism of clonazepam accelerated by carbamazepine, phenobarbitone and phenytoin

Cost : Tab 2 mg (10) Rs. 30.00 – 42.00

Acetazolamide ☆

It is a carbonic anhydrase inhibitor and is included in the class of diuretics. It has other metabolic effects as well.

I: It is a second line drug for both tonic clonic and partial seizures. It is

10. Drugs used in Neurological Disorders

occasionally helpful in atypical absence, atonic and tonic seizures. Other indications include raised intracranial tension, hydrocephalus and angle-closure glaucoma.

C/I: Renal hyperchloraemic acidosis, Addison's disease, sensitivity to sulphonamides, pregnancy and lactation

P/C: Avoid in severe renal impairment; pregnancy.

S/E: Paraesthesia in elderly, hypokalaemia, lack of appetite, drowsiness and depression; rashes and blood disorders occur rarely and renal calculi have been reported.

P/A: Tablet 250 mg.

Dose: Epilepsy and raised intracranial tension

Adult - 0.25 to 1 g daily in divided doses;

Children - 8 to 30 mg/kg daily; maximum 750 mg daily.

Glaucoma - 0.25 to 1 g daily in divided doses.

D/I: Potentiation of the action of folic acid antagonists, oral hypoglycemic agents, oral anticoagulants and severe reactions to sulphonamides.

Cost : Tab 250 mg (10) Rs. 9.00 – 14.00

Gabapentin

I: Adjunctive treatment of partial seizures with or without secondary generalisation not satisfactorily controlled with other antiepileptics.

C/I: Hypersensitivity

P/C: Avoid sudden withdrawal. The drug should be tapered off over at least 1 week.

S/E: Somnolence, dizziness, ataxia, tremor, diplopia, nausea and vomiting, also convulsions.

P/A: Capsule 300 mg and 400 mg.

Dose: 300 mg on first day, then 300 mg b.d. on second day, then 300 mg t.d.s. on third day, then increased according to response to 1.2 g daily (in 3 equally divided doses). Not recommended for children.

D/I: Reduced absorption with antacids; cimetidine may reduce gabapentine clearance

Cost : Caps 300 mg (20) Rs. 497.00 – 500.00

Lamotrigine

Is a phenyltriazine unrelated to currently available antiepileptic drugs. It acts by inhibiting the release of glutamate.

I: Anticonvulsant - adjunctive therapy in the treatment of partial seizures in adults with epilepsy.

C/I: Hypersensitivity, lactation

P/C : Hepatic and renal impairment, close monitoring during long term therapy is required, children below 16 years, elderly, pregnancy, during discontinuation of therapy.

S/E: Diplopia, drowsiness, dizziness, ataxia, headache, nausea and vomiting.

P/A: Tablets 25 mg, 100 mg, 150 mg, 200 mg.

Dose : Starting dose of 25 mg h.s. increasing in 25 mg/day increments at 2 week intervals to a maximum of 100 mg/day.

D/I: Valproic acid blocks the elimination of lamotrigine.

Cost : Tab 25 mg (10) Rs.0.00

10.2.1 Drugs used in status epilepticus

Status epilepticus should be treated initially with intravenous diazepam, used with caution because of the risk of respiratory depression.

In situations where facilities for resuscitation are not immediately available, diazepam is given by i.v. 10-20 mg at a rate of 1-2 mg/min, repeated if necessary after 30-60 min to a maximum dose of 100 mg in 24 hrs. This may be followed by i.v. upto a maximum 3mg/kg over 24 hrs.

For children 200 - 300 mcg/kg or 1 mg per year of age to a maximum of 40 mg in 24 hrs.

The drug can be administered as a rectal solution.

Prevention of recurrence :

For adults phenytoin sodium may be given by slow i.v., with ECG monitoring in a dose of 15-20 mg/kg at a rate of not more than 30-50 mg/min to a maximum of 1.5 g in 24 hrs.

In children 15-20 mg/kg at a rate of 0.5-1.5 mg/kg/min a maximum of 20mg/kg. i.m. use of phenytoin is not recommended (absorption is slow and erratic).

Alternatively, phenobarbitone sodium can be given

Adults : 10-15 mg/kg at a rate of not more than 100mg/min to a maximum of 1-2 g in 24 hrs i.v.

Children : 20mg/kg at the rate of 25-50 mg/min to a maximum of 40mg/kg .

Paraldehyde also remains a valuable drug in intractable status epileptics. It is given by deep i.m. as a single dose of 5-10 mL, maximum 20 mL daily with not more than 5 mL at any one site.

Children : up to 3 months 0.5 mL,

3-6 months 1 mL,

6-12 months 1.5 mL,

1-2 years 2 mL,

10. Drugs used in Neurological Disorders

3-5 years 3-4 mL,

6-12 years 5-6 mL.

By rectum, 5-10 mL, administered as a 10% enema in physiological saline.

When given rectally risk of respiratory depression is minimal and is therefore useful where facilities for resuscitation are poor.

Paraldehyde is no longer recommended by i.v. infusion.

If the above measures fail to control seizures, anaesthesia with thiopentone or non-barbiturate anaesthesia should be instituted with full intensive care support.

10.2.2 Febrile Convulsions

Brief febrile convulsions need only simple treatment such as tepid sponging, bathing, or antipyretic medication, e.g. paracetamol. Febrile convulsions lasting 3-5 minutes or longer, recurrent convulsions, or those occurring in a children at known risk for seizures must be treated more actively, as there is the possibility of resulting brain damage. Diazepam is the drug of choice given either by slow intravenous injection in a dose of 250 mcg/kg or preferably rectally in solution in a dose of 500 mcg/kg upto a maximum of 10 mg, repeated if necessary. The rectal route is preferred, as satisfactory absorption is much easier. Suppositories are not suitable because absorption is too slow.

Follow up therapy:

Vast majority of children get over the tendency for febrile convulsion by 5 years. A few may develop epileptic tendency and subsequent brain damage may occur. Such infants should be given long-term intermittent, or continuous antiepileptic medication.

10.3 DRUGS USED IN PARKINSONISM AND OTHER MOVEMENT DISORDERS

Parkinsonism is due to degeneration of the substantia nigra in the hindbrain and consequent loss of dopamine containing neurons in the nigrostriatal pathway. Drugs do not cure but greatly improve quality of life in this progressive disease. Two balanced systems are important in the extrapyramidal control of motor activity at the level of corpus striatum and substantia nigra. In one the neurotransmitter is acetylcholine; in the other it is dopamine. In Parkinson's disease, there is degenerative loss of nigrostriatal dopaminergic neurons and the symptoms of the disease are due to dopamine depletion. Other parts of the brain including the medulla, the hypothalamas and certain pathways to cerebral cortex are also effected giving rise to vomiting, suppression of prolactin secretion, etc. Different effects of dopaminergic drugs can be explained by activation of these systems, namely emesis, suppression of lactation and occasionally psychotic illness. The symptom triad of the disease is hypokinesia, rigidity, and tremor.

The aim of management of parkinsonism is restoration of dopaminergic/cholinergic balance.

This can be achieved by:

Reducing cholinergic activity by antimuscarinic (anticholinergic) drugs. This approach is most effective in the acute treatment of rigidity.

Enhancing dopaminergic activity by dopaminergic drugs which may-

- ♦ Replenish neuronal dopamine by supplying levodopa, which is its natural precursor; administration of dopamine itself is ineffective as it does not cross the blood-brain barrier.
- ♦ Prolong the action of dopamine through selective inhibition of its metabolism e.g: selegiline
- ♦ Act as dopamine agonists e.g : bromocriptine, lysuride, apomorphine.
- ♦ Release dopamine from stores and inhibit reuptake e.g : amantadine.

This approach is most effective against hypokinesia and rigidity and less effective in the treatment of tremor. /

Both approaches are effective in therapy and may usefully be combined.

Neuroleptics used to manage psychotic behavior act by blockade of dopamine receptors, they are also antinauseant, may sometimes cause galactorrhoea and can induce parkinsonism. Neuroleptic induced parkinsonism is alleviated by antimuscarinics, but not by levodopa or amantadine, because the neuroleptics block dopamine receptors via which these drugs act.

10.3.1 Dopaminergic drugs used in parkinsonism

Levodopa, used with a dopa-decarboxylase inhibitor, is the treatment of choice for patients disabled by idiopathic Parkinson's disease. It is less effective in elderly patients and in those with long-standing disease who may not tolerate a dose large enough to overcome the symptoms. It is less effective in patients with post-encephalitic parkinsonism disease who are also prone to suffer from blood toxicity more frequently.

Parkinsonism caused by generalised degenerative brain disease does not usually respond to levodopa. It should not be used for neuroleptic-induced parkinsonism.

Levodopa, the amino-acid precursor of dopamine, acts mainly by replenishing depleted striatal dopamine. It improves bradykinesia and rigidity more than tremor. It is generally administered in conjunction with an extracerebral dopa-decarboxylase inhibitor, carbidopa, which prevents the peripheral degradation of levodopa to dopamine but unlike levodopa, does not cross the blood-brain barrier.

10. Drugs used in Neurological Disorders

The ergot derivatives, bromocriptine, cabergoline, lisuride, and pergolide act by direct stimulation of surviving dopamine receptor. Although effective, they have no advantages over levodopa. They should be reserved for patients in whom levodopa alone is no longer adequate or who despite careful titration cannot tolerate levodopa. Ergot derivatives are sometimes useful in reducing 'off' periods and in ameliorating fluctuations in the later stage of Parkinson's disease. Their use is often limited by their side-effects and when used with levodopa, abnormal involuntary movements and confusional states are common; occasionally, ergot derivative may cause neuropsychiatric effects and retroperitoneal fibrosis.

Amantidine has modest antiparkinsonian effects. It improves mild bradykinetic disabilities as well as tremor and rigidity. Unfortunately only a small proportion of patients derives much benefit from this drug and tolerance to its effects occurs. However, it has the advantage of being relatively free from side-effects.

Levodopa ☆

I: All forms of parkinsonism except drug induced parkinsonism.

C/I: Closed-angle glaucoma.

P/C: Elderly, patients with ischaemic heart disease; cerebrovascular, psychiatric hepatic and renal disease, peptic ulcer and glaucoma.

S/E: Nausea and vomiting, postural hypotension, cardiac arrhythmias, exacerbation of angina, facial tics, choreoathetoid movements of limbs, anxiety, night mares, depression, psychosis and on prolonged use fluctuation in motor performance.

P/A: Tablet 500 mg

Dose: Initially 250-500 mg daily in divided doses after meals, o.d or b.d. and increased according to response 3-4 days to reach 3-4 g daily. Rarely higher dose of 6-8 g may be required.

D/I: Risk of arrhythmias with volatile anaesthetics, hypertensive crisis with MAO inhibitors, enhanced hypotensive effect with antihypertensives, antagonism of effect with antipsychotics, levodopa plasma concentration increased by metoclopramide. Absorption of levodopa may be reduced by iron. Effect of levodopa antagonised by pyridoxine.

Levodopa therapy should be initiated with low doses and gradually increased, by small increments, at intervals of 2 to 3 days. The aim is to improve mobility, withdrawal serious side effects.

Note : During the first 6 to 18 months of levodopa therapy there may be a slow improvement in the response of the patient which is maintained for 1½ to 2 years; thereafter a slow decline may occur. Particularly troublesome is the 'on-off' effect the incidence of which increases as the treatment progresses. This is characterized by fluctuations in performance with normal performance

during the 'on' period and weakness and akinesia lasting for 2 to 4 hrs during the 'off' period. 'End-of-dose' deterioration may also occur where the duration of benefit after each dose becomes progressively shorter. Modified-release preparations may help with 'end-of-dose' deterioration or nocturnal immobility and rigidity.

Cost : Tab 500 mg (10) Rs. 16.00 - 25.00

Selegiline is a monamine-oxidase-B inhibitor used in severe parkinsonism in conjunction with levodopa to reduce 'end-of-dose' deterioration. Early treatment with selegiline may delay the need for levodopa therapy.

Co-careldopa (Carbidopa + Levodopa) ☆

A mixture of carbidopa and levodopa.

I:/C/I: P/C:/S/E: D/I: See under levodopa and notes above.

P/A: Tablet carbidopa 10 mg + levodopa 100 mg, carbidopa 25 mg + levodopa 100 mg, carbidopa 25 mg + levodopa 250 mg, carbidopa 50 mg + levodopa 200 mg.

Dose: Expressed as levodopa, initially 100-125 mg t.d.s - q.d.s. adjusted according to response; usual maintenance dose 0.75-1.5 g daily in divided doses after food.

Note: When transferring patients from levodopa, 3 tablets of co-careldopa 25/250 should be substituted for 4 g levodopa; the levodopa should be discontinued 12 hours beforehand.

Cost : Tab (L.dopa 100mg, C.dopa 10 mg) (10) Rs. 25.00
(L.dopa 100mg, C.dopa 25mg) (10) Rs. 42.00

Amantidine Hydrochloride

I: Parkinson's disease (but not drug induced extrapyramidal symptoms); antiviral against influenza- A virus.

C/I: Epilepsy, history of gastric ulceration, severe renal impairment; pregnancy, breast-feeding.

P/C: Hepatic and renal impairment, congestive heart failure and elderly

S/E: Insomnia, dizziness, confusion, nightmares, and rarely hallucinations.

P/A: Capsule 100 mg

Dose: 100 mg daily increased after one week to 100 mg b.d. usually in conjunction with other treatment.

The last dose should be given before 4.00 PM Elderly over 65 years, less than 100 mg daily or 100 mg at intervals of more than 1 day.

D/I: Extrapyramidal side effects with methyldopa, metirosine (which is used in medical management of pheochromocytoma), reserpine,

10. Drugs used in Neurological Disorders

antipsychotics, tetrabenazine; increased antimuscarinic side effects with antimuscarinics.

Cost: Cap 100 mg (10) Rs. 30.00 – 32.00

Bromocriptine

I: Parkinsonism (but not drug - induced extrapyramidal symptoms).
Endocrine disorders such as galactorrhoea, cyclical benign breast disease, prolactinoma and acromegaly.

C/I: Hypersensitivity to bromocriptine or other ergot alkaloids, toxemia of pregnancy and hypertension in postpartum and puerperal women.

P/C: Serious mental disorders, cardiovascular disease or Raynaud's syndrome, and porphyria.

Not recommended for children under 15 years

S/E: Nausea, vomiting, constipation, and postural hypotension, confusion, delusions or hallucinations in high doses. After prolonged use, pleural effusion and retroperitoneal fibrosis.

P/A: Tablet 1.25 mg and 2.5 mg.

Dose: Parkinsonism

First week 1-1.25 mg at night, second week 2-2.5 mg at night, third week 2.5 mg b.d., fourth week 2.5 mg t.d.s. then increase by 2.5 mg every 3-14 days according to response to a usual range of 10-40 mg daily; taken with food.

Prevention and suppression of lactation

2.5 mg on 1st day (prevention) or daily for 2-3 days (suppression); then 2.5 mg b.d. for 14 days.

Hypogonadism/galactorrhoea, infertility

Initially 1 to 1.25 mg h.s, increased gradually; usual dose 7.5 mg daily in divided doses, increased if necessary to a maximum of 30 mg daily. Usual dose in infertility without hyperprolactinaemia, 2.5 mg b.d.

Cyclical benign breast disease and cyclical menstrual disorder (particularly breast pain)

1 to 1.25 mg h.s., increased gradually, usual dose 2.5 mg b.d.

Acromegaly

Initially 1-1.25 mg h.s., increase gradually to 5 mg every 6 h.

Prolactinoma

Initially, 1-1.25 mg h.s., increased gradually to 5 mg every 6 h
occasional patients may require up to 30 mg daily.

D/I: Antagonism of antipsychotic effect with antipsychotics. With

domperidone and metoclopramide antagonism of hypoprolactinaemic effect.

Cost: Tab 2.5 mg (10) Rs. 87.00 – 115.00

Selegiline

- I: Parkinson's disease or symptomatic parkinsonism (but not drug-induced extrapyramidal symptoms), either used alone (in early disease) or as an adjunct to levodopa therapy.
- C/I: Tardive dyskinesia adult onset Huntington's disease, levodopa psychosis.
- P/C: Peptic ulceration, uncontrolled hypertension, arrhythmias, angina, psychosis, pregnancy and breast-feeding, side effects of levodopa may be increased, concurrent levodopa dosage may need to be reduced by 20-50%.
- E: Hypotension, nausea and vomiting, confusion or psychosis, agitation, dry mouth, liver enzyme disturbances, sleep disturbances; difficulty in micturition and skin reactions reported.
- P/A: Tablet 5mg and 10 mg.
- Dose: 10 mg in morning, or 5 mg at breakfast and midday.
Elderly: to avoid initial confusion and agitation, it may be appropriate to start treatment with a dose of 2.5 mg daily.
- D/I: Fatal interactions with meperidine. Hyperpyrexia and CNS toxicity with pethidine. Hypertension and CNS excitation with fluoxetine.
- Cost: Tab 5 mg (10) Rs. 24.00 – 35.00

10.3.2 Antimuscarinic drugs used in Parkinsonism

Antimuscarinic drugs benefit parkinsonism by blocking acetylcholine receptors in the central nervous system, thereby partially, compensating for the imbalance created by decreased dopaminergic activity. Synthetic derivatives are now used orally. These include benzhexol, orphenadrine, benztropine, procyclidine and biperiden. These drugs produce modest improvements in tremor, rigidity, sialorrhea, muscular stiffness and leg cramps, but slight improvement of hypokinesia. They are effective in acute drug induced dystonias when given i.m. or i.v.

Benzhexol Hydrochloride

(Trihexyphenidyl hydrochloride)

- I: Parkinsonism; drug-induced extrapyramidal symptoms (but not tardive dyskinesia)
- C/I: Urinary retention, closed-angle glaucoma, and gastro-intestinal obstruction.
- P/C: Cardiovascular diseases, hepatic or renal impairment, elderly. This

10. Drugs used in Neurological Disorders

drugs may affect performance of skilled tasks including automobile driving.

S/E: Dry mouth, gastro-intestinal disturbances, dizziness, blurred vision; urinary retention and with high doses, mental confusion, excitement and psychiatric disturbances.

P/A: Tablet 2 mg

Dose: Adult : 1 mg daily, gradually increased to the usual maintenance dose of 5-15 mg daily given in 3-4 divided doses; elderly, 5 mg daily.

D/I: Many drugs have antimuscarinic effects. Concomitant use of such drugs can increase side effects such as dry mouth, urinary retention and constipation and confusion with elderly. Reduced absorption of ketoconazole. Increased antimuscarinic side effects with antihistaminics, antiarrhythmics, tricyclics, and MAOIs.

Antagonism of gastrointestinal effect with cisapride.

Cost: Tab 2 mg (10) Rs. 3.00 – 7.00

Biperiden

I, C/I, P/C, S/E, D/I: Same as for benzhexol hydrochloride.

P/A: Tablet 2 mg,

Injection 5 mg/mL

Dose: Oral: 1 mg b.d., gradually increased to 2 mg t.d.s.; usual maintenance dose 3-12 mg daily in divided doses; elderly 1 mg b.d.

Parenteral : i.m. or slow i.v. injection, 2.5-5 mg up to q.d.s.; elderly, the dose should not exceed 2.5 mg t.d.s. or q.d.s.

Cost: Tab 2 mg Rs 17.00

Inj 5mg/mL (1 mL) Rs 10.00

Orphenadrine Hydrochloride

I, C/I, P/C, S/E, D/I: Same as for benzhexol hydrochloride.

P/A: Tablet 50 mg

Dose: Adult : 150 mg daily in divided doses, gradually increased; maximum 400 mg daily, for elderly keep the dosage at 150 mg/day in divided doses.

Cost: Tab 50 mg (10) Rs. 13.00 – 14.00

Procyclidine Hydrochloride

I, C/I, S/E, Same as for benzhexol hydrochloride

P/C : Reduces threshold for seizures.

P/A: Tablet 2.5 mg, 5 mg

Dose: Oral : 2.5 mg t.d.s., gradually increased if necessary to the usual

maximum of 30 mg daily; elderly, 2.5 mg t.d.s.

D/I: With phenothiazines hyperpyrexia may occur especially in humid and hot weather. Additive anticholinergic effect with antihistamines, opiate antagonists, phenothiazines, tricyclic antidepressants, quinidine.

Cost: Tab 2.5 mg (10) Rs. 8.00 - 9.00

10.4 DRUGS USED IN ESSENTIAL TREMOR, CHOREA, TICS AND RELATED DISORDERS

Haloperidol may be useful in improving motor tics and related chorea. Propranolol or other beta-adrenoreceptor blocking drug may be useful in treating essential tremor or tremors associated with anxiety or thyrotoxicosis. Primidone in some cases provides relief from benign essential tremor; the dose should be increased only gradually to prevent rapid emergence of side effects.

Haloperidol

I: Motor tics, adjunctive treatment in chorea.

Dose: Oral : 0.5-1.5 mg t.d.s. adjusted according to response.

Primidone

I: Essential tremor; epilepsy

Dose: Essential tremor, initially 50 mg daily increased gradually over 2-3 weeks according to response; maximum 750 mg daily.

Propranolol

I: Essential tremor

Dose : Propranolol is given in a dosage of 40 mg b.d. or t.d.s., increased if necessary; 80 to 160 mg daily is usually required for maintenance.

10.5 DRUGS USED IN NAUSEA AND VERTIGO

Cinnarizine

This belongs to the class of piperazine derivative.

I: Vestibular disorders, such as vertigo, tinnitus, nausea and vomiting, Meniere's disease; motion sickness; peripheral vascular disease, Raynaud's syndrome

C/I;P/C; S/E: Drowsiness, occasional dry mouth and blurred vision; allergic skin reactions, fatigue, hypotension, extrapyramidal symptoms in elderly. To be avoided in porphyria, pregnancy and lactation.

P/A: Tablets 25 mg, 75mg.

Dose: Vestibular disorders, 30 mg t.d.s.,

For children 5-12 years - half adult dose.

10. Drugs used in Neurological Disorders

Motion sickness, 30 mg 2 h before travel, then 15 mg 8 h during journey if necessary. For children 5-12 years - half adult dose.

D/I: Alcohol enhances the CNS depressant effect, action of cinnarizine is potentiated by domperidone.

Cost: Tab 25mg (10) Rs 10.00

Cyclizine

It is a piperazine derivative.

I: Nausea, vomiting, labyrinthine vertigo, motion sickness.

C/I:, P/C:, S/E: Drowsiness, occasional dry mouth and blurred vision; cyclizine may aggravate heart failure.

P/A: Tablet 50 mg

Injection 50 mg/mL.

D/I: Same as cinnarizine.

Dose: Oral : cyclizine hydrochloride 50 mg up to t.d.s.

Parenteral : by i.m. or i.v. cyclizine lactate 50 mg t.d.s.

For children 6-12 years 25 mg,

Cost: Not freely available.

Dimenhydrinate

It is a theophylline derivative.

I: Nausea, vomiting, vertigo, motion sickness and labyrinthine disorders.

C/I:, P/C:, S/E:, D/I: Same as cyclizine. To be avoided in porphyria.

P/A: Tablet 50 mg,

Injection 50 mg/mL.

Liquid 5mg/mL

Dose: Oral 50-100 mg b.d - t.d.s.

Parenteral 50 mg i.m. every 4-6 h or i.v. in emergencies diluted.

1 mL in 10 mL normal saline

For children 1-6 years 12.5-25 mg, b.i.d - t.i.d.

7-12 years 25-50 mg.

Motion sickness first dose 30 min before journey.

Cost: Tab 50 mg (10) Rs. 10.00

Inj 50 mg/mL (5 x 1) Rs. 15.00

Promethazine Hydrochloride ☆

This is a phenothiazine group of drug.

I: Nausea, vomiting, labyrinthine vertigo, motion sickness;

symptomatic relief of allergy such as hay fever, urticaria; emergency treatment of anaphylactic reactions, night sedation, insomnia.

C/I; P/C; D/I: Epilepsy, prostatic hypertrophy, urinary retention, glaucoma, hepatic diseases and porphyria

S/E: Drowsiness, headache, psychomotor impairment, urinary retention, gastro-intestinal disturbances, hypersensitivity reactions, convulsions and extrapyramidal effects.

P/A: Tablet 10 mg, 25 mg,

Syrup 5mg/5mL

Elixir 5mg/5mL

Injection 2.5mg/mL

D/I: Same as cinnarizine

Dose: Prevention of motion sickness 25 mg elixir at h.s. on the night before travelling to be repeated the following morning if necessary.

For children 5-10 mg at night and following morning.

In allergy oral 25 mg at night increased to 50 mg or 10-20 mg b.d. or t.d.s.

For children 5-15 mg o.d.

By deep i.m. 25-50 mg, maximum 100 mg;

For children 6.25-12.5 mg.

In emergencies to be given by slow i.v. infusion, 25-50 mg. up to maximum 100 mg as a solution containing 2.5mg/mL diluted with water for injection.

Cost : Tab 25 mg	(10)	Rs. 5.00 – 8.00
Syrup 5 mg/ 5mL	(50 mL)	Rs. 8.00 – 10.00
Inj 25 mg/mL	(10 x 2mL)	Rs. 36.00 – 37.00

Chlorpromazine Hydrochloride ☆

This belongs to the class of phenothiazine.

I: Nausea and vomiting of terminal illness where other drugs have failed or are not available, intractable hiccup, hyperthermia, antipsychotics.

Dose: Oral: 10-25 mg every 4-6 h

Children : 1 – 5 years 500 mcg /kg every 4-6 h maximum of 40 mg o.d.,

6-12 years maximum 75 mg o.d.

Parenteral: By deep i.m. 25 mg initially then 25-50 mg every 3-4 h until vomiting stops;

For children 500 mcg/kg every 6-8 h.

10. Drugs used in Neurological Disorders

The maximum dose should not exceed 40 mg in children below 5 years and 75 mg in children below 12 years.

Prochlorperazine ✧

This belongs to the class of phenothiazine.

I: Severe nausea, vomiting, vertigo and labyrinthitis.

Dose: Oral : nausea and vomiting, acute attack, 20 mg initially then 10 mg after 2 h.

For prevention 5-10 mg b.d. or t.d.s.

For children over 10 kg - 250 mcg/kg b.d. or t.d.s. For smaller babies it should not be given.

Labyrinthine disorders - 5 mg t.d.s., gradually increased if necessary to 30 mg o.d. in divided doses, then reduced after several weeks to 5-10 mg o.d. This drug is not recommended for children.

Parenteral : by deep i.m., 12.5 mg when required, followed if necessary after 6 h by an oral dose.

Cost :	Tab 5 mg	(10)	Rs. 8.00 – 9.00
	Inj 12.5 mg/mL	(10x1 mL)	Rs. 42.00 – 43.00

Trifluoperazine

This belongs to the class of phenothiazine.

I: Severe nausea and vomiting

Dose: Oral, 2-4 mg o.d. in divided doses or as a single dose of modified release tablet; maximum 6 mg o.d.

For children 3-5 years up to 1 mg o.d.,
 6-12 years up to 4 mg o.d.

D/I: Same as chlorpromazine hydrochloride.

Cost : Tab 5 mg (10) Rs. 3.00 – 6.00

Domperidone ✧

It belongs to the class of benzimidazole derivatives.

I: Acute nausea and vomiting, non organic dyspepsia

C/I: Hypersensitivity, pregnancy, GI haemorrhage obstructive lesions of GIT, visceral perforation and after surgery.

P/C: Renal impairment, pregnancy and breast-feeding, not recommended for routine prophylaxis of postoperative vomiting or for chronic administration.

S/E: Reduced libido, rashes.

P/A Tablet 10 mg and
 Suspension 1mg/mL.

Drops 10 mg/mL.

Syrup 1 mg/mL.

Dose: Acute nausea and vomiting 10-20 mg every 4-8 h. Not recommended for children.

D/I: Opioid analgesics and antimuscarinics inhibit the effects on the gastro-intestinal tract. It antagonises the hypoprolactinaemic effect of bromocriptine

Cost :	Tab	10 mg	(10)	Rs. 18.00 – 20.00
	Susp	1 mg/mL	(30 mL)	Rs. 12.00 – 20.00
	Drop	10 mg/mL	(5 mL)	Rs. 13.00 - 15.00
	Syrup	1 mg/mL	(30 mL)	Rs. 20.00.

Metoclopramide Hydrochloride ☆

It is benzamide drug. Metoclopramide is a substituted benzamide with DA antagonistic activity.

I: Adults, nausea and vomiting particularly in gastro-intestinal disorders. To suppress nausea and vomiting in patients receiving anti cancer drugs or radiotherapy, migraine.

C/I: GI haemorrhage, mechanical obstruction, perforation of GI tract, hypersensitivity, phaeochromocytoma, parkinsonism, pyloric stenosis, previous history of dystonia.

P/C: Hepatic and renal impairment, elderly subjects, young adults, children, immediate postoperative period following gastrointestinal surgery (3-4 days), in patients with pheochromocytoma it may cause hypertensive crisis.

S/E: Extrapyramidal effects, hyperprolactinaemia, tardive dyskinesias, drowsiness, diarrhoea, and neuroleptic malignant syndrome.

P/A: Tablet 10 mg, 15 mg

Syrup 5mg/5mL,

Injection 5mg/mL.

Liquid 5 mg/mL.

Dose: Nausea and vomiting - adults 10 mg b.d. or q.d.s.

Oral :Young adults (15-20 years) 5-10 mg b.d. or q.d.s.

For children < 1 year, 1 mg b.d. Maximum daily oral dose 0.5 mg/kg

1-2 years, 1 mg b.d. or q.d.s.

3-4 years, 2 mg b.d. or q.d.s.

5-8 years, 2.5 mg b.d. or q.d.s.

9-14 years, 5 mg b.d. or q.d.s.

Nausea and vomiting associated with cancer chemotherapy

10. Drugs used in Neurological Disorders

2-4 mg /kg as an i.v. drip over 15-30 min.

Maintenance dose: 3-5mg/kg given over 8 h.

Maximum 10mg/kg/day.

D/I: Increased absorption of aspirin and paracetamol with enhancement of their activity. Opioid analgesics antagonise effect on gastrointestinal activity, increased risk of extrapyramidal effects with reserpine. Antimuscarinics, antipsychotic drugs, lithium and tetrabenazine antagonise gastrointestinal motility. The hypoprolactinaemic effect of bromocriptine is antagonised.

Cost :	Tab 10 mg	(10)	Rs. 5.00 – 7.00
	Inj 5 mg/mL	(2 mL)	Rs. 4.00 – 5.00
	Vial 5 mg/mL	(10 mL)	Rs. 8.00 – 12.00
	Liquid 5 mg/mL	(30 mL)	Rs. 13.00 – 14.00
	Syrup 5 mg/mL	(30 mL)	Rs. 5.00 – 12.00

Hyoscine Hydrobromide

It is a tropine alkaloid derivative with antimuscarinic activity.

I: Motion sickness, premedication for anaesthesia.

C/I: Closed angle glaucoma

P/C: Elderly, urinary retention, cardiac abnormalities, hepatic and renal impairment.

S/E: Drowsiness, dry mouth and urinary obstruction and changes in heart rate.

P/A: Tablet 10 mg

Injection 20mg/mL .

Dose: Oral : 10 mg 6-8 h,

Parenteral : 20 mg i.m./i.v. repeat if necessary after 30 min.

For conditions like motion sickness – 100 to 300 mcg, b.d or t.d.s is all that is required. Due to the availability of better drugs it is not used for this purpose.

For treatment of severe visceral spasmodic pain much higher dose of the order of 10-20 mg oral or 10-20 mg i.m./i.v. are required. This process may be required upto four times daily as necessary.

D/I: Increased incidence of side effects with tricyclics, monoamine oxidase inhibitors, antihistaminics, antipsychotics, amantadine. The effects of sublingual nitrates are reduced.

Cost :	Tab	10mg	(10)	Rs 13.00
	Inj	20mg/mL	(1mL)	Rs 5.00

Betahistine Dihydrochloride

It is an histamine analogue.

I: Vertigo, tinnitus and hearing loss associated with Meniere's disease

C/I: Phaeochromocytoma

P/C: Asthma, history of peptic ulcer; pregnancy and breast feeding.

S/E: Gastrointestinal disturbances, headache, rashes and pruritus.

P/A: Tablet 8 mg.

Dose: Initially 16 mg t.d.s. preferably with food; maintenance 24-48 mg o.d.

For children it is not recommended.

D/I: Antihistamine antagonises the effect.

Cost : Tab 8 mg (25) Rs. 60.00 – 62.00

CHAPTER 11 : DRUGS USED IN PSYCHIATRY

11.1. Antipsychotics

11.2. Antidepressants

11.3. Mood stabilizers

11.4. Anxiolytics

11.5. Sedatives and hypnotics

11.6. Drugs used in substance use disorders

11.7. Drugs used in drug induced movement disorders

11.8. Cerebral stimulants

11.1. ANTIPSYCHOTICS

These drugs were termed 'neuroleptics' or 'major tranquilizers'. These are group of drugs of diverse chemical nature used for the symptomatic treatment of psychoses, including schizophrenia, organic psychoses, manic phase of bipolar affective disorder and other serious psychotic illnesses.

Classification of Antipsychotics

I. Typical

1. Phenothiazines: Chlorpromazine, prochlorperazine, thioridazine, fluphenazine and trifluoperazine.
2. Thioxanthines: Flupenthixol
3. Butyrophenones: Haloperidol.
4. Dibenzoxazepines: Loxapine.
5. Diphenyl butylpiperidines: Pimozide

II. Atypical

1. Benzisoxazole: Risperidone
2. Dibenzodiazepines: Clozapine

11.1.1 Phenothiazines

Chlorpromazine Hydrochloride ☆

This is a very commonly used phenothiazine drug.

- I: Schizophrenia and other psychoses, mania, short term adjunctive management of anxiety, psychomotor agitation, induction of hypothermia, antiemetic and in terminal illness, intractable hiccups.

C/I: Comatose states, bone marrow depression and pheochromocytoma.

P/C: Cardiovascular and cerebrovascular disease, respiratory disease, parkinsonism, pregnancy, breast-feeding, renal and hepatic impairment, leucopenia, hypothyroidism, myasthenia gravis, prostatic hypertrophy, and angle-closure glaucoma.

S/E: Drowsiness, extrapyramidal symptoms such as drug induced parkinsonism, occasionally tardive dyskinesia, akathisia, hypothermia, apathy, pallor, nightmares, insomnia, depression and more rarely, agitation and convulsions.

Antimuscarinic symptoms may develop which include dryness of the mouth, constipation, difficulty with micturition, and blurring of vision; cardiovascular symptoms such as hypotension, tachycardia, and arrhythmias; respiratory depression.

Endocrine effects such as menstrual disturbances, galactorrhoea, gynaecomastia, impotence and weight gain.

Toxic effects such as leucopenia, leucocytosis, agranulocytosis and haemolytic anaemia, jaundice.

Neuroleptic malignant syndrome characterised by catatonia, stupor, fever unstable blood pressure, myoglobinuria and even fatal termination

Drug induced lupus erythematosus like syndrome, corneal and lens opacities

P/A: Tablets 10 mg, 25 mg, 50 mg, 100 mg, 200 mg,
Injection 25mg/mL

Dose: Schizophrenia and other psychoses

Oral - start initially with 25-50 mg t.d.s., or 75-150 mg at night, adjusted according to response.

The usual maintenance dose is 75-300 mg o.d., rarely up to 1 g o.d. may be required for psychoses

Elderly, one-third to half adult dose;

Children with schizophrenia and autism

1-5 years, 2 mg/kg/day upto a maximum of 40 mg o.d.;

6-12 years, third to half the adult dose maximum of 75 mg o.d.

Parenteral - by deep i.m. injection, given for the relief of acute symptoms (25-50 mg every 6-8 h)

Intractable hiccup - 25 to 50 mg t.d.s. or q.d.s. orally or by i.m. injection.

Induction of hypothermia - deep i.m. injection, 25-50 mg every 6-8 h.

D/I: Enhanced sedative effect with alcohol, anxiolytics and hypnotics enhanced hypotensive effect with anaesthetics and antihypertensives. Reduced absorption of chlorpromazine with antacids.

Antagonism of antipsychotic effect with dopaminergics. Cimetidine may enhance the effects of chlorpromazine.

Cost: Tab 25 mg (10) Rs. 5.00 – 7.00
Inj 25 mg/mL (2 mL) Rs. 5.00 – 6.00

Trifluoperazine Hydrochloride

I: Schizophrenia and other psychoses, psychomotor agitation, anxiety, antiemetic.

C/I:, P/C:, S/E:, D/I: Same as for chlorpromazine.

P/A: Tablets 1 mg, 5 mg, 10 mg.

Dose: Schizophrenia, other psychoses and psychomotor agitation

Start initially with 5 mg b.d., or 10 mg o.d. in modified release form and increase by 5 mg after 1 week according to the response to a maximum of 20 mg/day in divided doses.

Children up to 12 years - start initially with doses up to 5 mg o.d. in divided doses and adjust according to response, age and body weight not exceeding 15 mg/day.

Anxiety 2-4 mg o.d. in divided doses increased if necessary upto 6 mg o.d.;

Children 3-5 years upto 1 mg o.d.,
6-12 years upto 4 mg o.d.

Cost: Tab 5 mg (10) Rs. 3.00 - 6.00

Thioridazine Hydrochloride

I: Schizophrenia and other psychoses, psychomotor agitation, anxiety.

C/I:, P/C:, S/E:, D/I: Same as for chlorpromazine. Additional side effects include delayed ejaculation, pigmentary retinopathy and lenticular opacity if dose is more than 800 mg/day.

P/A: Tablets 5 mg, 10 mg, 25 mg, 50 mg and 100 mg.

Dose: Oral: schizophrenia and other psychoses 150-600 mg o.d. initially in divided doses, up to a maximum of 800 mg daily in hospitalized patients.

For psychomotor agitation, excitement and violent behavior 75-200 mg o.d.

Anxiety, and agitation in the elderly, 30-100 mg o.d.

Children with severe mental or behavioral problems only :

1-5 years, 1mg/kg day,

5-12 years, 75-150 mg/day and in severe cases, up to 300 mg day.

Cost : Tab 50 mg(10) Rs. 19.00 – 30.00

Fluphenazine Hydrochloride

I: Schizophrenia and other psychoses, mania, short term adjunctive management of severe anxiety, psychomotor agitation, excitement and violent, dangerously impulsive behaviour.

C/I:,P/C:, S/E:, D/I: Same as for chlorpromazine.

P/A: Tablet 1 mg, 2.5 mg, 5 mg

Injection 25 mg/mL contain oily solution of fluphenazine decanoate for depot use.

Dose: Schizophrenia and other psychoses

Oral : 2.5 -10 mg o.d. in 2-3 divided doses; adjusted according to response to 20 mg o.d.; doses above 20 mg (10 mg in elderly) should be given cautiously.

Parenteral: 25 mg as deep i.m. injection once in 2 - 4 weeks.

Anxiety, agitation and excitement

Oral: initially 1 mg b.d., increased as necessary to 2 mg b.d.

Cost : Tab 1 mg (10) Rs. 7.00

Inj 25 mg/mL (1 mL) Rs. 24.00 - 30.00

Prochlorperazine Maleate ☆

I: Schizophrenia and other psychoses, mania, severe anxiety, nausea, vomiting, vertigo, labyrinthine disorders.

C/I:,P/C:, S/E:, D/I: Same as for chlorpromazine.

P/A: Tablets 5 mg, 25-mg

Injection 12.5 mg/mL.

Dose: Schizophrenia and other psychosis

Oral: mania - start with 12.5 mg b.d. for 7 days and adjust at intervals of 4-7 days to reach the usual dose of 75-100 mg o.d. according to response; anxiety - 15 to 20 mg o.d. in divided doses upto a maximum of 40 mg.

Children over 10 kg 250 mcg/kg b.d. or t.d.s.

Parenteral: deep i.m. injection 12.5 mg b.d., t.d.s.or o.d.

Nausea and vomiting

Oral: acute attack - 20 mg initially and then 10 mg after 2 h if oral dose is tolerated and retained.

prevention - 5 to 10 mg b.d. or t.d.s.;

Parenteral: i.m. 12.5 mg initially and followed if necessary after 6 h by an oral dose

Labyrinthine disorders - 5 mg t.d.s., gradually increased upto 30 mg o.d. and then reduced after several weeks to the maintenance dose of 5-10 mg o.d.

Cost: Tab 5 mg (10) Rs. 8.00 - 9.00

Inj 12.5 mg/mL (10x1 mL) Rs. 40.00 - 43.00

11.1.2. Thioxanthines

Flupenthixol Decanoate

I: Schizophrenia and other psychoses, particularly with apathy and withdrawal but not mania or psychomotor hyperactivity, depression.

C/I: P/C: S/E: D/I: Same as for chlorpromazine.

P/A: Tablets 0.5 mg, 1 mg, 3mg

Injection 20 mg/1mL, 40 mg/2mL.

Dose: Psychoses: Initially 3-9 mg b.d. adjusted according to the response upto a maximum of 18 mg o.d.;

Elderly - start initially with quarter to half adult dose;

For children this drug is not recommended.

Depression: Initially 1 mg in the morning, increased after 1 week to 2 mg if necessary to maximum 3 mg o.d., doses above 2 mg are divided into 2 portions, second dose not after 4 p.m. Discontinue if no response after 1 week at maximum dosage.

Elderly 0.5 mg to 2 mg/day

Parenteral dose: Schizophrenia and other psychoses, 20-40 mg deep i.m. as depot injection every 2-4 weeks.

Cost: Tab 1 mg (10) Rs. 25.00

Inj 40 mg (2 mL) Rs. 147.00

11.1.3 Butyrophenones

Haloperidol ☆

I: Schizophrenia and other psychoses, mania, short term adjunctive management of psychomotor agitation, excitement and violent or dangerously impulsive behaviour, severe anxiety, intractable hiccup, motor tics.

C/I: P/C: S/E: D/I: Same as for chlorpromazine hydrochloride.

P/A: Tablets 0.25 mg, 1 mg, 1.5 mg, 5 mg, 10 mg, 20 mg,

Injection 5mg/1 mL,

Drops 10 mg/mL

Syrup 2 mg/mL, 10 mg/mL,

Depot Injection 50 mg/mL as decanoate.

Dose: Schizophrenia and other psychoses

Oral : start initially with 1.5 -3 mg b.d. or t.d.s. or 3-5 mg b.d. or t.d.s. in severely affected or resistant patients. In resistant schizophrenia up to 100mg (rarely upto 120 mg) o.d. may be needed. Maintenance dose is adjusted as the lowest effective dose which may be as low as 5-10 mg o.d.;

Elderly initially half adult dose;

Children initially 25-50 mcg/kg in two divided doses upto a maximum of 10 mg o.d. in two divided doses.

Adolescents upto 30 mg o.d., exceptionally upto 60 mg.

Parenteral : by i.m. injection, 2-10 mg, subsequent doses being given every 4-8 h according to response upto a total maximum of 60 mg. Severely disturbed patients may require initial dose of upto 30 mg;

Anxiety - adults 0.5 mg b.d.;

Hiccup - 1.5 mg t.d.s., adjusted according to response.

Nausea and vomiting 0.5-2 mg.

Motor tics and adjunctive treatment of chorea - orally, 0.5-1.5 mg t.d.s., adjusted according to the response. Upto 10 mg o.d. or more may be needed.

Children with Gilles de la tourette syndrome upto 10 mg daily.

Cost : Tab 1.5 mg (10) Rs. 8.00 - 11.00

Inj 5 mg/mL (1 mL) Rs. 5.00 - 10.00

11.1.4 Dibenzoxazepines

Loxapine

I: Acute and chronic psychoses

C/I:, P/C:, S/E:, D/I: Same as for chlorpromazine hydrochloride

P/A: Capsules 10 mg, 25 mg, 50 mg

Liquid 25 mg/mL.

Dose: Oral: initially 20-50 mg o.d. in 2 divided doses, increased as necessary over 7-10 days to 60-100 mg o.d. upto a maximum of 250 mg in 2-4 divided doses. The usual maintenance dose of 20- 100 mg o.d.

Cost : Caps 50 mg (6) Rs. 73.00 - 74.00

Liquid 25 mg/mL (60 mL) Rs. 257.00 - 258.00

11.1.5 Diphenyl butylpiperidines

Pimozide

I: Schizophrenia, monosymptomatic hypochondriacal psychoses, paranoid psychoses, mania.

C/I:, P/C:, S/E:, D/I: Same as for chlorpromazine, but less sedating. It is contraindicated in breast-feeding. Serious cardiac arrhythmias may occur and therefore ECG has to be taken before treatment in all patients and repeated during the course.

P/A: Tablets 2mg, 4 mg, 10 mg.

Dose: Schizophrenia.

Oral : initially 10 mg o.d., adjusted according to response with

11. Drugs Used in Psychiatry

increments of 2 - 4 mg at intervals of 1 week or more upto a maximum of 20 mg o.d. For prevention of relapse the maintenance dose may vary from 2-20 mg/day.

For elderly, start with half the adult dose.

Monosymptomatic hypochondriacal psychoses and paranoid psychoses.

Start initially with 2 mg o.d., and adjust according to response with increments of 2 - 4 mg at intervals of 1 week or more upto a maximum of 16 mg o.d.

Elderly, half usual starting dose.

Mania, hypomania, short-term adjunctive management of excitement and psychomotor agitation.

Start initially 2-4 mg o.d. and adjust according to response with increments of 2-4 mg at intervals of 1 week or more upto a maximum of 20 mg o.d.

Cost: Tab 2 mg (10) Rs. 12.00 – 35.00

11.1.6 Benzisoxazole

Risperidone

I: Acute and chronic psychoses.

C/I:, P/C:, S/E:, D/I: Same as for chlorpromazine.

P/A: Tablets 1 mg, 2 mg, 3 mg, 4 mg

Liquid 1 mg/mL

Dose: Oral : 2 mg in 1-2 divided doses on first day, and increased to 4 mg on second day, 6 mg in 1-2 divided doses on third day upto the usual range of 4-8 mg o.d., Upto 16 mg o.d. may be given exceptionally only if benefit is considered to outweigh the risk.

Elderly, 0.5 mg b.d., increased in increments of 0.5 mg b.d. to 1-2 mg b.d.

For children under 15 years not recommended.

Cost : Tab 2 mg (10) 27.00 – 35.00

11.1.7 Dibenzodiazepine

Clozapine

I: Schizophrenia in patients unresponsive to, or intolerant of conventional antipsychotic drugs.

C/I: Severe cardiac disease; history of drug-induced neutropenia or agranulocytosis; bone marrow disorders; alcoholic and toxic psychoses; history of circulatory collapse or paralytic ileus; drug intoxication, coma or severe CNS depression, uncontrolled epilepsy, pregnancy and breast-feeding.

P/C: Leucocyte and differential blood counts must be normal before treatment and must be monitored weekly for first 18 weeks, then fortnightly.

Avoid drugs which depress leucopoiesis, withdraw treatment if leucocyte count falls below $3000/\text{mm}^3$ or absolute neutrophil count falls below $1500/\text{mm}^3$. Patients should report any infections, hepatic or renal impairment, epilepsy, cardiovascular disorders, prostatic enlargement, glaucoma, paralytic ileus. Avoid abrupt withdrawal, avoid in children.

S/E: High incidence of antimuscarinic symptoms; extrapyramidal symptoms may occur less frequently, neutropenia and potentially fatal agranulocytosis, fever, headache, dizziness, urinary incontinence, priapism, pericarditis, myocarditis, delirium, hypotension, sialorrhea, skin rashes and convulsions (if dosage is above 800 mg/day).

P/A: Tablets 25 mg, 100 mg

Dose: 12.5 mg o.d. or b.d. on first day, then 25-50 mg on second day, then increase gradually in steps of 25-50 mg over 7 - 14 days to 300 mg o.d. in divided doses. Larger dose upto 200 mg o.d. may be taken as a single dose at h.s Further increased in steps of 50-100 mg once or twice weekly may be required.

Usual antipsychotic dose 200-450 mg o.d. upto a maximum of 900 mg o.d. Subsequent maintenance dose of 150-300 mg.

Elderly, 12.5 mg once on first day subsequent adjustments restricted to 25 mg o.d.

D/I: Clozapine cause agranulocytosis when used concurrently with drugs associated with a substantial potentials for causing agranulocytosis, such as co-trimoxazole, chloramphenicol, sulphonamides, penicillamine, cytotoxics or carbamazepines.

Cost : Tab 100 mg (10) Rs. 50.00

11.2 ANTIDEPRESSANTS

Antidepressants are drugs which can elevate the mood in depressive illness. Conventional antidepressants are of two types : monoamine oxidase inhibitors (MAOIs) and tricyclic and related antidepressants.

Tricyclic antidepressants and the selective serotonin reuptake inhibitors (SSRIs) are preferred to the MAOIs because they are more effective and do not show the dangerous interactions with some foods and drugs like the latter.

Routine use of few or more antidepressants simultaneously is not desirable. Compound preparations of an antidepressant and an anxiolytic are not ideal because the dosage of the individual components cannot be adjusted separately. Whereas antidepressants have to be given continuously over several months, anxiolytics are usually required only for short-term periods.

General principles of management

The patient must be closely supervised, especially in the early weeks of treatment to detect any suicidal tendency. Only small quantities of antidepressant drugs should be dispensed at any one time since they are likely to be used for suicidal poisoning.

Symptomatic improvement starts at about 2 weeks. Thereafter the dose should be maintained at the optimum level for at least 4-6 months after the depression has been controlled. Treatment should not be withdrawn abruptly since the symptoms are likely to recur. The natural history of depression suggests that remission usually occurs after 3 months to one year or more. In recurrent depression prophylactic maintenance therapy with an effective dose may have to be continued for several years.

In patients who do not promptly respond to antidepressants the diagnosis, dosage, compliance, and possible continuation of psychosocial or physical aggravating causes should all be carefully reviewed. Alternate treatment modalities may be successful.

WITHDRAWAL OF DRUGS : Reduction in dosage should be done gradually over a period of several weeks.

11.2.1. Tricyclic antidepressants

Amitriptyline Hydrochloride ☆

- I: Depressive illness particularly where sedation is required. Nocturnal enuresis in children, Prophylaxis of migraine
- C/I: Recent myocardial infarction, arrhythmias particularly heart block, manic phase of depression, severe liver disease.
- P/C: Cardiac disease, history of epilepsy, pregnancy and breast feeding, elderly subjects, hepatic impairment, pheochromocytoma, history of mania, psychoses, angle-closure glaucoma, history of urinary retention. Abrupt withdrawal should be avoided. It should be used with caution in subjects requiring anaesthesia. Drowsiness may affect skilled tasks such as driving and handling of machinery during work. The effects of alcohol are enhanced.
- S/E: Dry mouth, sedation, blurred vision, constipation, nausea, urinary retention; cardiovascular side effects such as arrhythmias, postural hypotension, tachycardia, hypersensitivity reactions including urticaria and photosensitivity; hypomania, mania, confusion, interference with sexual function, increased appetite and weight gain, endocrine side-effects such as testicular enlargement, gynaecomastia, galactorrhoea; neurological features such as tremors, convulsions, movement disorders and dyskinesias, fever, agranulocytosis and jaundice.
- P/A: Tablet 10 mg, 25 mg, 50 mg, 75 mg.
- Dose: Depressive illness :

Oral: Start initially with 25 mg daily and increase gradually to a maximum of 150 mg either as single dose h.s. or in divided doses. The usual maintenance dose is 50-100 mg o.d., For the elderly and adolescents the average dose is smaller (30- 75 mg/day).

For migrane prophylaxis initially 10 mg as a single bedtime dose, to be increased gradually if necessary up to 100 mg.

Nocturnal enuresis :

Children 7-10 years 10 to 20 mg h.s., 11-16 years 25 to 50 mg h.s. The maximum period of treatment including gradual withdrawal is upto 3 months. Full physical examination to exclude organic causes is mandatory before starting treatment.

D/I: All the tricyclic antidepressants have similar drug interactions which may produce serious adverse effects, enhanced sedative effect with alcohol, CNS excitation and hypertension with MAOIs, antagonism of antidepressant effect with antiepileptics, hypotensive effect enhanced with antihypertensives, increased sedative effect with antihistaminics, reduction of effect of sublingual nitrates, oral contraceptives antagonise antidepressant effect, potentiation of hypertension and arrhythmias with adrenaline.

Cost : Tab 10 mg (10) Rs. 3.00 – 10.00

Amoxapine

I: Depressive illness

C/I:,P/C:,S/E:, D/I: Similar to amitriptyline. Additional side effects include tardive dyskinesia, akathisia,menstrual irregularities, breast enlargement and galactorrhoea.

P/A: Tablet 50 mg and 100 mg

Dose: Initially 100-150 mg o.d. in divided doses or as a single dose at h.s., increased gradually to a maximum of 300 mg o.d. The usual maintenance dose is 150-250 mg.

For the elderly the dose is initially 25 mg b.d. increased as is necessary after 5-7 days to a maximum of 50 mg t.d.s.

Cost : Tab 50 mg(10) Rs. 30.00

Clomipramine Hydrochloride ☆

I: Depressive illness, phobic and obsessional states; adjunctive treatment of cataplesy associated with narcolepsy.

C/I:, P/C:, S/E:, D/I: Same as for amitriptyline hydrochloride

P/A: Tablets 10 mg, 25 mg and 50 mg.

Sustained Release - Tablet 75 mg,

Capsule 10 mg and 25 mg.

Dose: Initially 10 mg o.d., increased gradually as necessary to 30-150 mg

o.d. in divided doses or as a single dose at h.s. upto a maximum of 250 mg o.d. The usual maintenance dose is 30-50 mg o.d. For the elderly start with 10 mg o.d. and increase over 2 weeks to 100-150 mg o.d.

For adjunctive treatment of cataplesy associated with narcolepsy, start with 10 mg o.d. and gradually increase to 10-75 mg/day until satisfactory response is obtained.

Cost : Cap 25 mg (10) Rs. 29.00 – 35.00

Tab 25 mg (10) Rs. 27.00 - 30.00

Dothiepin Hydrochloride

I: Depressive illness particularly where sedation is required

C/I; P/C; S/E; D/I: Same as for amitriptyline hydrochloride

P/A: Tablet 25 mg and 75 mg.

Capsules 25 mg

Dose: Initially 25 mg daily increased gradually as necessary to 150 mg daily, and even up to 225 mg daily at times.

For the elderly 75 mg may be sufficient.

Cost : Tab 25 mg(10) Rs. 14.00

Doxepin Hydrochloride

I: Depressive illness, particularly where sedation is required.

C/I;P/C;S/E;D/I: Similar to amitriptyline hydrochloride. This drug should be avoided during breast feeding.

P/A:Capsule 10 mg, 25 mg and 75 mg.

Dose: Start with 30 mg o.d., or in divided doses or as a single dose h.s., and increase as necessary to maximum of 300 mg o.d., in 3 divided doses of 100 mg each. The usual range is 30-300 mg o.d. In the majority 30-50 mg o.d. may be adequate. For the elderly initial dose is 10-50 mg o.d. This drug is not recommended for children.

Cost : Cap 25 mg (10) Rs. 18.00 – 28.00

Imipramine Hydrochloride ☆

I: Depressive illness, nocturnal enuresis in children

C/I;P/C;S/E;D/I: Similar to amitriptyline hydrochloride, but the drug is less sedative.

P/A: Tablet 25 mg and 75 mg,

Capsule 25 mg and 75 mg.

Dose: Depressive illness: Start with upto 25 mg daily and increased gradually upto 150-200 mg, even upto 300 mg in hospitalized patients. Upto 150 mg may be given as a single dose h.s. The usual maintenance dose is 50-100 mg o.d.

For the elderly, start initially with 10 mg o.d. and increase gradually to 30-50 mg o.d.

Nocturnal enuresis

For children upto 7 years, 25 mg,

8 - 11 years, 25-50 mg

Over 11 years, 50-75 mg single dose given

h.s. The maximum period of treatment including gradual withdrawal should not exceed 3 months.

Cost : Tab 25 mg (10) Rs. 5.00 - 6.00

Caps 25 mg (10) Rs. 6.00 - 7.00

Nortriptyline Hydrochloride

I: Depressive illness, nocturnal enuresis in children

C/I:,P/C:,S/E:,D/I: Similar to amitriptyline hydrochloride but less sedating.

P/A: Tablet 25 mg

Dose: Depressive illness: Start with low dose initially and increase as is necessary to 75 - 100 mg o.d. in divided doses or as a single dose.

For adolescent and elderly 30-50 mg o.d. in divided doses.

Not recommended for children.

Nocturnal enuresis :

For children below 12 years 25 mg, over 12 years 50 mg h.s.

The maximum period of treatment including gradual withdrawal should not exceed 3 months.

Cost : Tab 25 mg(10) Rs 10.00

Trimipramine Maleate

I: Depressive illness, particularly where sedation is required.

C/I:,P/C:,S/E:,D/I: Similar to amitriptyline hydrochloride

P/A: Tablet 10 mg and 25 mg

Dose: 50-75 mg o.d. as a single dose 2 hrs before sleep or 25 mg midday and 50 mg evening. It is increased as required to a maximum of 300 mg o.d., and maintained for 4-6 weeks. Thereafter the dose is reduced to usual maintenance dose of 75-100 mg o.d.;

For the elderly start with 10-25 mg t.d.s. and maintain at half adult maintenance dose.

Cost : Tab 25 mg(10) Rs. 12.00

Mianserin Hydrochloride

I: Depressive illness, particularly where sedation is required.

C/I:,P/C:,S/E:, D/I: Similar to amitriptyline hydrochloride. Adverse side effects

11. Drugs Used in Psychiatry

include leucopenia, agranulocytosis, aplastic anaemia particularly in the elderly, jaundice, arthritis, arthralgia and rarely autonomic disturbances including antimuscarinic effects and postural hypertension. A full blood count should be done every 4 weeks during the first 3 months of treatment and subsequent clinical monitoring should continue regularly. Treatment should be stopped and a full blood count obtained if fever, sore throat, stomatitis or other signs of agranulocytosis develop.

P/A: Tablet 10 mg, 20 mg and 30 mg.

Dose: Start with 30-40 mg (elderly 30 mg) o.d. in divided doses or a single dose h.s., increase gradually as is necessary to the usual dose range of 30-90 mg.

This drug is not recommended for children.

Cost : Tab 20 mg(10) Rs. 28.00 – 50.00

Trazodone Hydrochloride

I: Depressive illness, particularly where sedation is required.

C/I:,P/C:,S/E:, D/I : Similar to amitriptyline hydrochloride, but fewer antimuscarinic action and cardio vascular effects. Rarely priapism may develop, in which case the drug has to be discontinued abruptly.

P/A: Tablet and Capsule 25 mg, 50 mg and 100 mg.

Dose: Initially 50 mg (elderly 25 mg) o.d. in divided doses after food or a single dose h.s. to be increased to 300 mg o.d. if necessary.

In hospitalized patients the dose can be increased upto a maximum of 600 mg o.d. in divided doses.

This drug is not recommended for children.

Cost : Tab 50 mg(10) Rs. 20.00 - 30.00

11.2.2 Serotonin-specific reuptake inhibitors (SSRI)

They are also known as selective serotonin reuptake inhibitors. They have no effect on the reuptake of dopamine or norepinephrine.

Fluoxetine

I: Depression, obsessive compulsive disorder (OCD), panic disorders, anxiety disorders.

C/I: Pregnancy, lactation.

P/C: Use with caution in patients with seizures and diabetes.

S/E: Insomnia, anorexia, nausea, diarrhoea, headache, nervousness, anxiety, seizures in high doses, sexual dysfunction.

P/A: Capsule 20 mg.

Suspension 20 mg/ 5 mL

Dose : Depression - 20 mg/day.

OCD - 60 mg/day.

D/I: Increased sedation with other drugs having sedative effect on central nervous system. Produces agitation, restlessness and gastric distress with tryptophan. Produces changes in serum lithium level. Produces sedation, dry mouth and constipation with other antidepressants.

Cost : Cap 20 mg (10) Rs. 13.00 - 25.00

Susp 20 mg/5 mL (60 mL) Rs. 25.00 - 35.00

Sertraline

I:, P/C :, S/E :, D/I : Same as for fluoxetine.

C/I: Hypersensitivity, pregnancy, lactation, history of drug abuse, hepatic or renal impairment, seizure disorders.

P/A: Tablet 50 mg

Dose : 100 - 150 mg/day.

Cost : Tab 50 mg (10) Rs. 25.00 - 30.00

11.3 MOOD STABILIZERS

11.3.1 Lithium Carbonate

This is a very common drug used in psychiatric practice

I: Treatment and prophylaxis of mania and manic-depressive illness and recurrent depression; aggressive or self-mutilating behavior.

C/I: Renal failure and cardiac failure, disturbed electrolyte balance, major surgery, pregnancy and lactation, sick-sinus syndrome.

P/C: Avoid in renal impairment, cardiac failure, and Addison's disease, caution in pregnancy, breast-feeding, myasthenia gravis, surgery.

S/E: Gastro-intestinal disturbances, fine tremor, polyuria and polydipsia, and oedema.

Hypothyroidism, hypokalaemia. Signs of lithium intoxication are blurred vision, anorexia, vomiting and diarrhoea, muscle weakness, increasing CNS disturbances and these require withdrawal of treatment. With severe overdose convulsions, toxic psychoses, coma and occasionally death may occur.

P/A: Tablets 150 mg, 300 mg, 450 mg,

Capsule 300 mg.

Dose: 600-800 mg/day in divided doses till a blood level of 1-1.55 mEq/L is achieved. Maintenance level should aim at 0.7-1 mEq/L. Serum levels should be maintained during treatment at this level. Levels above 1.5 mEq/L are dangerous.

D/I: Lithium toxicity is made worse by sodium depletion therefore

concurrent use of diuretics particularly thiazides is hazardous and should be avoided.

Cost: Tab 300 mg (10) Rs. 8.00 – 11.00

11.3.2. Iminostilbenes

Carbamazepine ☆

This is primarily an antiepileptic drug.

I: It may be used for prophylaxis of manic depressive illness unresponsive to lithium.

Dose: Initially 400 mg o.d. in divided doses increased until symptoms are controlled.

The dosage range from 400-600 mg o.d.

Upto a maximum of 1.6 g o.d. may be required in rare cases.

11.3.3. Valproic acid derivatives

Sodium Valproate (see section 10.2)

11.3.4. Calcium channel blockers

Verapamil (See section 5.7.4)

Nifedipine (see section 5.7.4)

Diltiazem (see section 5.7.4)

11.4. ANXIOLYTICS

Moderate anxiety is a normal and even useful response to life events. But inappropriate, excessive or chronic anxiety is disabling, especially where the cause cannot be removed. Anxiety may also occur without apparent exogenous cause and those who suffer from such floating anxiety deserve help. Non-drug therapy such as counseling, relaxing practices and the like are ideal and many get relief by these measures. But drugs are often required for patients having high level of anxiety.

11.4.1 Benzodiazepines

Benzodiazepines now dominate antianxiety medications. In patients whose complaints are primarily of somatic or autonomic symptoms of anxiety rather than of anxiety itself, a beta-adrenoreceptor blocking drug can give benefit. A sedative antidepressant like amitryptiline should be chosen if there is depression with anxiety. Drugs in this group include diazepam, alprazolam, chlordiazepoxide, lorazepam and oxazepam.

Diazepam

I: Short-term use in anxiety or insomnia, adjunct in alcohol withdrawal; status epilepticus and febrile convulsion.

C/I: Respiratory depression, acute respiratory failure, severe hepatic impairment.

P/C: Respiratory disease, myasthenia gravis, pregnancy and breast feeding, hepatic and renal impairment.

S/E: Drowsiness, confusion and ataxia, amnesia, dependence, paradoxical increase in aggression.

P/A: Tablets 2mg, 5 mg, 10 mg

Capsule 2mg, 5mg, 10 mg, 15 mg

Syrup 2mg/5mL,

Injection 5mg/mL.

Injection (emulsion) 5mg/mL for i.v. injection or as infusion,

Suppository 2mg.

Dose: Anxiety

Oral - 2 mg t.d.s. increased if necessary to 15-30 mg o.d. in divided doses;

Elderly half the adult dose;

Insomnia associated with anxiety 5-15 mg h.s.;

Children with night terrors and somnambulism, 1-5 mg h.s.

Parenteral - slow i.v. injection into a large vein at a rate of not more than 5 mg/min, for the management of severe acute anxiety, control of acute panic attacks, and acute alcohol withdrawal. 10 mg may be repeated, if necessary after 4 h. Injection (i.m.) can be given but absorption from the site is erratic and the are unpredictable.

Rectal - for acute anxiety and agitation, as rectal solution or suppositories 10 mg. If necessary a further 10mg may be given after at least 10 min.; elderly 5 mg.

D/I: Isoniazid, omeprazole and disulfiram inhibit metabolism of diazepam and other benzodiazepines. Benzodiazepines antagonise the effect of levodopa.

Cost :	Tab 10 mg	(10)	Rs. 4.00 – 10.00
	Cap10 mg	(10)	Rs. 12. 00- 13.00
	Inj 5 mg/mL	(2 mL)	Rs. 5.00 – 7.00

Alprazolam

I: For the short term management of anxiety states.

C/I, P/C, S/E: Same as for diazepam.

P/A: Tablets 0.25 mg, 0.5 mg, 1 mg

Sustained Release (SR) 1.5 mg

Dose: 250-500 mcg t.d.s.

Elderly 250 mcg b.d. – t.d.s., increased if necessary to a total of 3 mg o.d.;

D/I: Same as for diazepam

Cost : Tab 0.5 mg (10) Rs. 4.00 – 15.00

Chlordiazepoxide

I: For short term use in anxiety.

Adjunct in acute alcohol withdrawal symptoms.

C/I:, P/C:, S/E:, D/I: Same as diazepam.

P/A: Tablets 10 mg and 25 mg

Dose: Anxiety 10 mg t.d.s. increased if necessary to 60-100 mg o.d. in divided doses;

For elderly half adult dose.

Adjunct in acute alcohol withdrawal symptom: 10- 50 mg q.d.s., gradually reducing over 7-14 days.

Cost : Tab 25 mg (10) Rs. 10.00 – 12.00

Lorazepam

I: Short term use in anxiety or insomnia;

Status epilepticus

C/I:, P/C:, S/E:, D/I: Same as for diazepam.

P/A: Tablets 1 mg, 2 mg.

Injection 2mg/mL

Dose: Oral : anxiety 1-6 mg o.d. in divided doses;

Elderly start at 1-2 mg/day in divided doses.

Insomnia associated with anxiety 1 to 2 mg h.s.

Parenteral : i.m. or i.v. injection into a large vein. This is indicated in acute panic attacks, dose is 20-30 mcg/kg, repeated every 6 h if necessary.

Cost : Tab 1 mg (10) Rs. 5.00 – 7.00

Inj 2 mg/mL (2 mL) Rs. 7.00 – 8.00

Oxazepam

This is a short acting drug with a half life of 6-10 hrs compared to diazepam which has a half life of 60 h.

I: Short term use in anxiety

C/I:, P/C:, S/E:, D/I: As for diazepam; short acting.

P/A: Tablets 15 mg, 30 mg

Dose: Anxiety, 15-30 mg

Elderly 10-20 mg t.d.s or q.d.s.

Insomnia associated with anxiety 15-25 mg, upto a maximum of 50 mg h.s.

Cost : Tab 15 mg(10) Rs. 6.00 – 7.00

11.4.2 Buspirone Hydrochloride

This belongs to a different class of drugs. The exact site and mechanism of action of buspirone have not been determined. Buspirone acts at specific serotonin producing receptors and on brain D₂-dopamine receptors. It has good anxiolytic action, without any anticonvulsant or muscle relaxant activity and does not appear to cause physical dependence or significant sedation. Response to treatment is slow and the full effect may be evident in 2 weeks.

I: Anxiety

C/I: Epilepsy, severe hepatic or renal impairment, pregnancy and breast-feeding.

P/C: Presence of hepatic or renal impairment

S/E: Nausea, dizziness, headache, nervousness, excitement, tachycardia and confusion.

P/A: Tablet 5mg and 10 mg.

Dose: Initially 5 mg b.d. or t.d.s., increased every 2-3 days if needed. The usual dose ranges from 15-30 mg o.d. upto a maximum of 45 mg o.d.

Cost: Tab 5 mg (10) Rs. 6.00 – 9.00

11.5 SEDATIVES AND HYPNOTICS

Hypnotics are drugs that induce sleep. About one third of adults have difficulty in sleeping and half of them consider this as serious. Management of insomnia involves detailed analysis of particular circumstances. Before a hypnotic is prescribed the cause of the insomnia should be established, and where possible, underlying factors should be treated. A drug is not always appropriate but if required should be chosen for its suitable therapeutic effect and used for brief periods. Prescription for a hypnotic is justified for a few days or up to one month to treat sleeplessness due to anxiety, provided there is good reason to expect the cause to be removed either by changes in environment or by treatment. But where there is a persistent insomnia or a personality disorder a prescription is not justified because tolerance develops, dependence is likely.

Generally a hypnotic is best taken on going to bed or a few minutes before. All hypnotics induce tolerance and dependence. Abrupt withdrawal may produce insomnia and even convulsions. In chronic users the withdrawal should be gradual.

Children: Except for occasional use such as for night terrors or somnambulism regular use is not justified.

Elderly: Hypnotics should be avoided in the elderly since they may become ataxic and confused and therefore sustain injury.

Common drugs in this class are benzodiazepines, chloral and its derivatives and antihistamines

11.5.1 Benzodiazepines

Benzodiazepines used as hypnotics include the long acting drugs such as nitrazepam, flunitrazepam and flurazepam. They may give rise to residual effects on the following day. Repeated doses tend to be cumulative.

Loprazolam, lormetazepam and temazepam act for shorter periods and they have little or no hangover effect. Withdrawal phenomena however are more common with the short-acting benzodiazepines.

Benzodiazepine anxiolytics such as diazepam given as a single dose at night may also be used as hypnotics. However, there may be drowsiness after waking up in the morning.

Nitrazepam

I: Short term use in insomnia

C/I: Myaesthesia gravis, respiratory depression, acute pulmonary insufficiency, severe hepatic impairment.

P/C: Respiratory disease, muscle weakness, hepatic and renal impairment.

S/E: Drowsiness, confusion and ataxia, dependence.

P/A: Tablet 2.5 mg, 5 mg, 10 mg

Dose 5-10 mg h.s.

Elderly 2.5-5 mg;

D/I: Enhanced sedative effect with alcohol and opioid analgesics, enhanced hypotensive effect with antihypertensives.

Cost : Tab 2.5 mg (10) Rs. 5.00 – 6.00

Flurazepam Monohydrochloride

I, C/I, P/C, S/E, D/I: Same as for nitrazepam.

P/A: Capsule 15 mg

Dose: 15 - 30 mg h.s.

Elderly 15 mg.

Cost : Cap 15 mg (10) Rs. 15.00 – 20.00

11.5.2 Chloral and derivatives

Chloral Hydrate and derivatives were formerly popular hypnotics for children. At present these drugs are used less frequently. There is no convincing evidence that they are particularly useful in the elderly and their role as hypnotics is now very limited. Triclofos causes fewer gastro-intestinal upsets than chloral hydrate.

Chloral Hydrate

I: Short term use in insomnia

- C/I: Cardiac disease, gastritis, hepatic or renal impairment; pregnancy and breast-feeding; porphyria.
- P/C: Respiratory disease, avoid prolonged use, avoid contact with skin and mucous membranes.
- S/E: Gastric irritation, abdominal distention and flatulence, vertigo, ataxia, rashes, headache, excitement, delirium, leucopenia, dependance.
- P/A: Not commercially available.
- Dose: 0.5 g-1 g (maximum 2g), with plenty of water at h.s.;
Children 30-50 mg/kg upto a maximum single dose of 1 g.
- Cost: Not commercially available. It can be dispensed under special circumstances. Fixed combinations of chloral hydrate with other drugs is banned.

Triclofos Sodium

I;C/I, P/C;S/E: Same as for chloral hydrate

Less gastric irritation.

P/A: Liquid 500mg /5mL

Dose: 10-20 mL containing 1-2 g h.s.
children up to 1 year 25-30 mg/kg,
1-5 years, 2.5-5 mL
6-12 years, 5-10 mL

D/I: General sedative interactions as for benzodiazepines, other anxiolytics and hypnotics.

Anticoagulant effect of nicoumalone and warfarin is enhanced.

Cost: Liquid 500 mg / 5 mL. (60 mL) Rs. 38.00 – 40.00

11.5.3 Non-benzodiazepines

Zopiclone

Zopiclone is an imidazopyridine. Although not a benzodiazepine it acts on the same receptors as benzodiazepines. Zopiclone has a short duration of action for 5-6 hrs with little or no hangover effect.

I: Short term use in insomnia

C/I: Myasthenia gravis, respiratory failure, severe sleep apnoea syndrome, hepatic impairment, pregnancy and lactation.

P/C: Pregnancy, hepatic and renal insufficiency. Duration of treatment with zopiclone should not exceed 4 weeks.

S/E: Bitter or metallic taste; gastro-intestinal disturbances including nausea and vomiting, drowsiness, incoordination, headache, hypersensitivity reactions, hallucinations, amnesia and behavioral disturbances.

P/A: Tablet 7.5 mg.

Dose : 7.5 mg h.s.

Elderly 3.75 mg h.s. increased if necessary.

D/I: General sedative interactions as for benzodiazepines and other anxiolytics and hypnotics.

Cost : Tab 7.5 mg (10) Rs. 38.00 – 75.00

11.5.4 Antihistamines active primarily on the CNS

Antihistamines are drugs which act by blocking the peripheral effects of histamine and other vasoactive substances or inhibiting their release and actions. They are primarily indicated for this effect on allergic reactions- both acute and long term. Several drugs in this group include promethazine, trimeprazine, dimenhydrinate, chlorpheniramine, cyclizine, astemizole, cetirizine, terfenadine and others. They all have got antihistaminic activity and as a side effect, sedation, which differs in intensity.

Antihistamines are not primarily hypnotics, still drugs such as promethazine hydrochloride are occasionally used for insomnia.

Promethazine Hydrochloride

I: Night sedation and insomnia, other indications include various forms of allergic reactions.

P/A: Tablets 10 mg and 25 mg,

Elixir, Syrup 5mg/5mL

Injection 25 mg/mL.

Dose: Oral - 25 mg at night, increased to 50 mg.

Children under 2 years, it should be used with caution,

2-5 years, 15-20 mg h.s.,

5-10 years, 10-25 mg h.s.

Parenteral - 25 to 50 mg deep i.m. injection(maximum 100mg),

Children 5-10 years 6.25-12.5 mg i.m. Slow i.v. injection (in emergencies) 25-50mg (upto100mg).

Parenteral dose is indicated in severe allergy and drug induced dystonia.

Cost: Tab 25 mg (10) Rs. 6.00 – 9.00

Syrup 5 mg/5 mL (50 mL) Rs. 8.00 – 9.00

Inj 25 mg/mL (10 x 2 mL) Rs. 36.00 – 37.00

11.6. DRUGS USED IN SUBSTANCE USE DISORDERS

Primary treatment of alcohol dependence consist of proper clinical and psychiatric examination to detect the underlying causes for addiction and the removal of all correctable causes. Drug treatment is only an adjunct to methods

like group therapy, counseling, behaviour modification and others.

11.6.1 Alcohol abuse

Disulfiram

Disulfiram is used as an adjunct in the treatment of chronic alcohol dependence. It gives rise to extremely unpleasant systemic reactions after the ingestion of even small amounts of alcohol because it leads to accumulation of acetaldehyde in the body. Reactions include flushing of the face, throbbing headache, palpitations, tachycardia, vomiting, hypotension, and collapse. Even the small amounts of alcohol included in many oral medicines may be sufficient to provoke a reaction. It is advisable for patients to carry a card warning the danger of administration of alcohol.

I: Adjunct in the treatment of chronic alcohol dependence.

C/I: Cardiac failure, coronary artery disease and history of cerebrovascular accident, hypertension, psychoses, pregnancy and breast-feeding.

P/C: Ensure that alcohol is not consumed for at least 24 h before initiating treatment, hepatic and renal impairment, respiratory disease, diabetes mellitus, epilepsy.

S/E: Drowsiness and fatigue; nausea and vomiting, reduced libido, rarely psychotic reactions.

P/A: Tablet 250 mg.

Dose: 1 g as a single dose on first day, reduced over 4 days to 0.75g to 0.25g o.d.; should not be continued for longer than 6 months without review.

D/I: Psychotic reaction with metronidazole, inhibition of metabolism of tricyclic antidepressants. Inhibition of metabolism of phenytoin. Inhibition of metabolism of benzodiazepines, leading to enhanced sedative effect.

Cost : Tab 250 mg (10) Rs. 7.00 – 11.00

11.6.2. Opioid abuse

Naltrexone

It is an opioid antagonists competitively binding opioid receptors.

I: Opioid dependence, adjunctive treatment in chronic alcoholism.

C/I: Concurrent use of opioids, hepatic failure, acute opioid withdrawal, as therapeutic opioid analgesics.

P/C: Use with caution in pregnancy, lactation, hepatic and renal impairment.

S/E: Nausea, vomiting, abdominal pain, sweating, lacrymation, dizziness, rash, reversible thrombocytopenia purpura

P/A: Tablet 50 mg

Dose: Opioid dependence - 50 mg daily. Once stabilized, 3 doses a week.
Alcoholism - 50 mg daily.

D/I: Concurrent use of hepatotoxic drugs increases the risk of hepatic dysfunction.

Cost: Tab 50 mg(10) Rs. 620.00

Naloxone

I: Opioid dependence, respiratory depression due to opioids.

C/I: Hypersensitivity.

P/C: Use with caution in pregnancy, lactation. Administer cautiously to persons dependent on opioids.

S/E: Seizures, pulmonary oedema. Abrupt reversal may cause nausea, vomiting, sweating, tachycardia and increased BP.

P/A: Injection 20 mcg/mL, 400 mcg/mL.

Dose: Narcotic overdose - 0.4 to 2 mg i.v. repeated at 2 - 3 min intervals.
Maximum 10 mg.

Children : 0.01 mg/kg i.v. initially and to be repeated if needed.

Neonates - 0.01 mg/kg i.v., i.m. or s.c. initially, and to be repeated if needed.

D/I: Enhances analgesia with buprenorphine, reverses alcohol intoxication.

Cost: Inj 20 mcg/mL (5 x 2 mL amp) Rs. 150.00

Clonidine (see section 5.7.6)

Used in opiate withdrawal.

11.7 DRUGS USED IN DRUG INDUCED MOVEMENT DISORDERS

11.7.1. Anticholinergics

Trihexyphenidyl (benzhexol) (see section 10.3.2)

Procyclidine (see section 10.3.2)

Benztropine (see section 10.3.2)

Biperiden (see section 10.3.2)

11.7.2 Amantadine (see section 10.3.1)

11.7.3 Propranolol (see section 5.7.3)

11.8 CEREBRAL STIMULANTS

Methyl phenidate

I: Attention deficit hyperactivity disorder (ADHD), narcolepsy.

- C/I: Hypersensitivity, anxiety, glaucoma, motortics, history of drug dependence or alcohols, epilepsy, hypertension and psychosis.
- P/C: Gradual dosage reduction necessary to avoid withdrawal symptoms.
- S/E: Hypertension, tachycardia, angina, arthralgia, dyskinesia, fever, thrombocytopenia purpura, anorexia, dizziness, vomiting, headache.
- P/A: Tablet 5mg, 10mg, 20 mg.
- Dose: 5-20 mg b.d. - t.d.s. after meals.
- D/I: Additive CNS stimulation with other CNS stimulation producing medication. Increased anticholinergic effect with other anticholinergic medication. Hypotensive effect of diuretics and antihypertensives are reduced. With monoamine oxidase inhibitors causes hypertensive crisis. Potentiates pressor effect of vasopressors when used concurrently with methylphenidate
- Cost: Not freely available.

Dextroamphetamine

- I: Attention deficit hyperactivity disorder (ADHD), narcolepsy.
- C/I: Pregnancy, lactation, hypersensitivity, agitated states, arteriosclerosis, glaucoma, hypertension, hyperthyroidism, history of drug abuse.
- P/C: Gradual dosage reduction necessary to avoid withdrawal symptoms. Caution if dizziness or euphoria occurs. Avoid driving automobiles or operating machinery while on therapy.
- S/E: Irregular heart beats, allergic reactions, chest pain, CNS stimulation, cardiomyopathy, increase in BP, nausea, vomiting, diarrhoea, dizziness, loss of appetite, abdominal pain.
- P/A: Capsules 5mg., 10mg., 15 mg.
Tablets 5mg, 10 mg.
- Dose: ADHD - 2.5 to 5mg once or twice a day, increased by 2.5-5 mg a day at 1 week interval. Narcolepsy - 5 to 60 mg/day.
- D/I: Increased risk of ventricular arrhythmias with inhalation anaesthetics. Severe arrhythmias, tachycardia or hypertension with tricyclic antidepressants. Reduced hypotensive effect of diuretics and antihypertensives. Increased risk of hypertension and excessive bradycardia and possible heart block with beta adrenergic blocking agents. Additive CNS stimulation with other CNS stimulation producing medications. Increased risk of cardiac arrhythmias with digitalis, levodopa and monoamine oxidase inhibitors.
- Cost: Not freely available.

Pemoline

- I: Attention deficit hyperactivity disorder (ADHD).

11. Drugs Used in Psychiatry

C/I: Hypersensitivity, hepatic and renal function impairment, psychosis, tics.

P/C: Gradual dosage reduction necessary to avoid withdrawal symptoms.

S/E: Anorexia, insomnia, weight loss, dizziness, drowsiness, irritability, mental depression, skin rash, nausea.

P/A: Tablet 18.75mg, 37.5mg, 75 mg

Dose: 37.5 mg single dose in the morning increased by 18.75 mg a day at one week interval (maximum 112.5 mg/day).

D/I: Increased effectiveness of anticonvulsants, additive CNS stimulation with other CNS stimulation producing medications.

Cost: Not freely available.

CHAPTER 12: DRUGS USED IN DISEASES OF KIDNEY AND URINARY TRACT

1. Diuretics
2. Immunosuppressive therapy
3. Drugs used in renal hypertension (Refer guideline)
4. Anti microbial therapy of urinary tract infections (Refer guideline)
5. Treatment of ARF and CRF (Refer guideline)
6. Medical treatment of urolithiasis
7. Drugs used in voiding dysfunction (Abnormalities of Micturation)
8. Drug nephrotoxicity and dosage in renal failure

Renal parenchymal diseases are broadly classified as glomerular and tubulointerstitial. Aetiologically 2/3 of all renal diseases are immune mediated and therefore immune modifying drugs are of great use.

Glomerular diseases often manifest with combination of proteinuria, haematuria, oedema, oliguria and hypertension. The various clinical syndromes are acute glomerulonephritis, nephrotic syndrome, rapidly progressive glomerulonephritis and chronic glomerulonephritis. Tubulointerstitial nephritis may be acute or chronic. Functional derangement of the kidney manifests as either acute or chronic renal failure of varying severity.

12.1 DIURETICS

Diuretics are mainly used for the treatment of oedema - renal, cardiac, hepatic. They lead to renal excretion of sodium, potassium and water in varying proportions. They lower blood pressure and therefore they are employed either as primary or as adjuvant drugs in the treatment of hypertension.

Commonly used diuretics are:

- Thiazide diuretics
- Loop diuretics
- Potassium sparing diuretics.
- Osmotic diuretics.
- Carbonic anhydrase Inhibitors.

12.1.1 Thiazide diuretics

Moderately potent diuretic, inhibit sodium resorption at distal convoluted tubule. Act within 1-2 hrs and most diuretics of them have a duration of action of 12-24 hrs. Single oral dosage is beneficial in the long term management of hypertension.

Hydrochlorothiazide ✧

- I: Congestive cardiac failure, nephrotic syndrome, ascites, systemic hypertension.

12. Drugs Used in Diseases of Kidney and Urinary Tract

C/I: Hypokalemia, hyponatremia, moderate and severe renal impairment, Addison's disease.

P/C: Hypokalemia, pregnancy, diabetes, gout, hyperlipidemia, hepatic and renal impairment, potentiates the effects of other antihypertensive drugs.

S/E: Postural hypotension, rash, impotence, fatigue, cramps, diarrhoea, nausea. On prolonged use dyslipidemia, hyperuricemia, hyperglycemia and hypokalemia can occur.

P/A: Tablets 50 mg

Dose : 25 - 100 mg daily.

D/I: Increase in serum lithium. NSAID's reduce the diuretic effect. Digoxin toxicity occurs if hypokalemia is present.

This drug is presently available at present only in combination with antihypertensive and potassium sparing diuretics.

Chlorthalidone ☆

I;C/I; P/C; S/E; D/I: Similar to hydrochlorothiazide but longer duration of action.

P/A: Tablets 100 mg.

Dose: Oedema: 50 - 100 mg daily.

Hypertension: 25 -50 mg daily.

Note: It is better to supplement oral potassium in doses of 1-2 g b.d. or t.d.s. along with thiazides , when used for prolonged periods

Cost : Tab 100 mg (10) Rs. 24.00 - 25.00

Indapamide

This is a weak diuretic. It potentiates the action of other standard antihypertensive drugs

I: Systemic hypertension

C/I: Recent CVA, severe liver damage.

P/C: Renal impairment, gout, hypokalemia, pregnancy, digoxin administration.

S/E: Muscle cramps, fatigue, hypokalemia, headache, postural hypotension, impotence, thrombocytopenia, hyperglycemia, erythema multiforme.

P/A: Tablets 2.5 mg

Dose: 2.5 mg daily for systemic hypertension.

D/I: Same as hydrochlorothiazide.

Cost : Tab 2.5 mg (10) Rs. 21.00 - 38.00

Xipamide

- I: Systemic hypertension, mild to moderate oedema.
- C/I: Allergy to sulfa drugs, pregnancy, renal or hepatic failure, refractory hypokalemia.
- P/C: Diabetes, gout, SLE, liver diseases.
- S/E: Hypocalcemia, paralysis, fatigue, cramps, GI upsets, lethargy.
- P/A: Tablets 20 mg
- Dose: Oedema due to a variety of causes; start with 40mg/day reducing to 20 mg /day according to patient response.
Hypertension: 20 mg daily as a single dose.
- D/I: Same as hydrochlorothiazide.
- Cost: Tab 20 mg (10) Rs. 25.00 - 26.00

Other Thiazides

Currently not available in India. Useful adjuncts in treatment of hypertension.

Bendrofluazide

- I, C/I, P/C, S/E: Same as chlorthiazide.
- P/A: Tablets 2.5 mg, 5 mg.
- Dose: Oedema: 5-10 mg daily
Maintenance: 5-10mg 1-3 times weekly.
Hypertension: 2.5 mg daily.

Hydroflumethiazide

- I, C/I, P/C, S/E: Same as chlorthiazide.
- P/A: Tablets 50 mg.
- Dose: Oedema: 50-200 mg daily
Maintenance: 25-50mg on alternate days.
Hypertension: 25-50 mg daily.

Polythiazide

- I, C/I, P/C, S/E: Same as chlorthiazide.
- P/A: Tablets 1mg.
- Dose: Oedema: 1-4 mg daily
Maintenance: 5-10mg
Hypertension: 0.5 mg

Metolazone

- I, C/I, P/C, S/E: Same as chlorthiazide.

P/A: Tablet 5 mg.

Dose: Oedema: 5-10 mg daily

20-80 mg in resistant oedemas

Profound diuresis with concomitant loop diuretic- monitor closely.

Note: *Thiazides are also used for calcium stone disease.*

12.1.2 Loop diuretics

Compared to thiazide diuretics, loop diuretics are more potent. The diuresis is dose dependant. They also possess vasodilator property. Inhibits reabsorption of sodium chloride at the thick ascending limb of loop of Henle. They are more effective in the management of oedematous states and acute pulmonary oedema but are not suitable drugs for systemic hypertension, where a less potent but more prolonged diuretic action such as that of thiazides is more advantageous. Rapid onset of action following both oral (within 1 hour) and parenteral (i.m. or i.v. peak action within 30 min, action is completed within 6 hours). When given i.v. the vasodilator action which is also responsible for the relief of dyspnoea in acute cardiac failure, starts immediately. In renal failure large doses are required.

Frusemide (furosemide) ☆

This is the most common loop diuretic currently in use.

I: Oedematous states, oliguria due to renal failure, acute pulmonary oedema, incipient acute renal failure

C/I: Severe sodium and water depletion, allergy to sulfonamide, Addisons disease.

P/C: Pregnancy, severe hepatic dysfunction, hypovolemia, hypokalemia, diabetes, gout, lower urinary tract obstruction.

S/E: Hypokalemia, hyponatremia, hypomagnesemia, postural hypotension, hyperuricemia, hyper glycemia, hypertriglyceredemia, tinnitus, cramps, rash.

P/A: Tablets 40 mg, 100 mg, up to 500 mg

Injection 20 mg/mL 2 mL vials

Dose: Oral tablets

Oedema: 40mg daily, maintenance 20-40mg daily, resistant oedema 80-120mg daily.

Children 1-3mg/kg/day.

Oliguria and renal failure: Higher doses in presence of renal failure. Initially 250mg daily may be stepped up in increments of 125-250mg up to a maximum dose of 2g.

Slow intravenous injection or intramuscular injection

i.v. rate not exceeding 4mg/min, 20- 40 mg initially, increase to 80-120 mg if necessary

Child 0.5 – 1.5mg/kg.

May be given by intramuscular route in situations where venous access is not obtained. The onset of action is delayed when given i.m.

Intravenous infusion

250mg over 1 h followed by 500mg in 2 h in oliguric renal failure up to 1g can be repeated every 24 h. This mode enables titration of dose and is thus beneficial in acute renal failure.

D/I: Furosemide potentiates antihypertensive action of other drugs, especially ACE inhibitors and alpha blockers. When administered concurrently with aminoglycosides the ototoxicity of the latter is increased. Serum lithium levels are increased. NSAID's decrease the diuretic effect.

Cost :	Tab	40 mg	(10)	Rs. 3.00 - 4.00
		500 mg	(10)	Rs. 30.00 - 35.00
	Inj	20 mg/mL(amp)	(10 x 2 mL)	Rs. 30.00 - 40.00

Note: It is better to use frusemide in oedema states and thiazide diuretics in systemic hypertension

For acute oliguric renal failure and in incipient renal failure, vials containing larger doses upto 250mg are available. Potassium supplements are required except in patients with renal failure. Prolonged use in chronic oedema- beneficial to combine with potassium sparing diuretic.

Bumetanide

I, C/I, P/C, D/I: Similar to frusemide.

S/E: Similar to frusemide, myalgia is common when used in high doses.

P/A: Tablets 1 mg

Dose: Oral, 1 - 2 mg per day in single or divided doses.

D/I: Interaction with aminoglycosides increases potential for ototoxicity. Drugs with nephrotoxic potential should be avoided. When given with lithium salts it precipitates lithium toxicity,
It potentiates the action of antihypertensives.

Cost: Tab 1 mg (10) Rs. 5.00 - 6.00

Ethacrynic acid

I, C/I, P/C, S/E, D/I : Same as furosemide, deafness is more common and this limits its use.

P/A & Dose: Inj 50 mg ampoules.

Tab 50 mg; 50 - 100 mg daily.

Cost: Not freely available.

12. Drugs Used in Diseases of Kidney and Urinary Tract

Torsemide

I, C/I, P/C, S/E, D/I : Same as furosemide. Avoid in pregnancy and breast feeding.

P/A: Not freely available

Dose: Oedema: 5mg o.d., 20-40 mg in resistant oedema.

Hypertension : 2.5 mg

Slow i.v. injection 4mg/min, 10-20 mg daily. Maximum dose 200mg/day in renal failure.

12.1.3 Potassium sparing diuretics

Major adverse side effect of thiazides and loop diuretics is hypokalemia. Potassium sparing diuretics do not cause hypokalemia and therefore they can be given singly or in combination with thiazides or loop diuretics. Their clinical effectiveness as diuretics is considerably less in comparison to frusemide. Potassium sparing diuretics are:

Aldosterone antagonists - spironolactone, amiloride, triamterene.

Spironolactone ☆

This potassium sparing diuretic is a competitive inhibitor of aldosterone.

I: Oedema and ascites of cirrhosis, nephrotic syndrome and congestive heart failure. Used along with thiazides to counteract potassium losing effect. Drug of choice in primary hyperaldosteronism.

C/I: Moderate and severe hyperkalemia, renal failure.

P/C: Chronic hepatic or renal disease, Addison's disease, hyperkalemia.

S/E: Gynecomastia, gastrointestinal side effects, impotence, menstrual irregularities, lethargy, rash, headache.

P/A: Tablets 25 mg, 100 mg

Dose: 25 mg 6 h upto 200 mg/day

This dose may be increased upto 400 mg / day in divided doses in selected cases.

D/I: It increases serum digoxin levels. Aspirin blocks the action of spironolactone. When NSAIDs are given concurrently with spironolactone this may lead to acute renal failure.

Cost: Tab 25 mg (10) Rs. 13.00 - 14.00

Triamterene

I: It is indicated in oedematous states, in combination with thiazides or loop diuretics, when potassium loss is to be minimized. Uncontrolled use may lead to hyperkalemia.

C/I: Hyperkalemia, renal failure.

P/C: Monitor plasma urea and potassium particularly in the elderly and in renal impairment.

S/E: GI disturbances, hyperkalemia, hyponatremia, photosensitivity, renal failure.

P/A: Combination tablet (triamterene 50 mg, frusemide 20 mg).

Dose: 150 - 250 mg daily, 50 mg in combination with thiazides.

D/I: Increases digoxin and lithium levels.

Cost: Tab triamterene 50 mg, frusemide 20 mg (10) Rs. 12.00 - 13.00

Amiloride

This is a potassium sparing diuretic used in combination with loop diuretics or thiazide.

I: Chronic oedematous states especially for in prolonged administration.

C/I: Hyperkalemia, hypersensitivity.

P/C: Pregnancy, diabetes mellitus.

S/E: Rash, dry mouth, GI side effects, hypokalemia, hyponatremia.

P/A: Combination tablets (frusemide 40 mg and amiloride hydrochloride 5 mg).

Dose: 5 mg - 10 mg/day.

D/I: Increases lithium levels and causes lithium toxicity. ACE inhibitors increase the risk of hyperkalemia.

Cost: Tab (frusemide 40 mg, amiloride hydrochloride 5 mg) (10) Rs.10.00-12.00.

12.1.4 Osmotic diuretics

Mannitol

I: Prevention of ARF in major cardiovascular surgery, enhancing urine flow in prerenal ARF after volume replacement.

Dose: 150 - 300 mL of 20% solution i.v. given over 10 - 20 min immediately prior to cross clamping of aorta, going on cardiac pulmonary and after adequate restoration of volume in hypovolemic states.

12.1.5 Carbonic Anhydrase Inhibitors

Acetazolamide

Seldom used for its diuretics action.

12.2 IMMUNOSUPPRESSIVE THERAPY

Corticosteroids

Corticosteroids are widely used as immunosuppressants in many immune mediated primary and secondary glomerular diseases and in renal transplantation. It inhibits interleukin-1(IL-1), T-helper cell activation, antibody production and also has anti inflammatory properties.

12. Drugs Used in Diseases of Kidney and Urinary Tract

Prednisolone

Prednisolone is the preferred corticosteroid for oral immunosuppression, because of its lesser suppressive effect on the hypothalamopituitary axis.

- I:** Nephrotic syndrome produced by minimal change disease and membranous nephropathy, lupus nephritis, other autoimmune disorders, vasculitis and renal transplantation.

Dose : Nephrotic syndrome

In adults: 1mg/kg/day or 2mg/kg/alternate day is recommended

In children : 2 mg/kg or 40mg/m² daily for 4 to 8 weeks, followed by alternate day therapy for a similar duration. Maintenance therapy in low dose of 0.1 to 0.2 mg on alternate days indicated in membranous nephropathy and steroid dependent minimal change disease for a period of 6 months.

Lupus nephritis

2 mg/kg bw for 4 - 8 weeks followed by 0.2 mg/kg bw maintenance 3 to 5 years.

Renal transplant

1 mg/kg to start, taper to 0.1 mg/kg by 3 - 6 months and continue life long. Usually combined with azathioprine and cyclosporine.

Methyl Prednisolone

Intravenous infusion of methyl prednisolone in high doses of upto 1 g daily for 3 - 5 days is called steroid pulse therapy and is used for early response in severely ill patients

- I:** Severe renal disease due to SLE, vasculitis, crescentic nephritis and severe acute interstitial nephritis with renal failure, acute transplant rejection.

C/I: Peptic ulcer, acute psychosis, Cushing's syndrome, herpes simplex, keratitis, infections, lactation.

P/C: Diabetes, pregnancy, seizure disorder. To be used by specialist only.

S/E: Besides the usual steroid side effects, acute hyperglycemia, hypokalemia, infections, and convulsions are more frequently encountered. Bolus injections may produce sudden cardiac death.

P/A: Injection methyl prednisolone sodium succinate and methyl prednisolone acetate in aqueous solution. 500 mg 1 g vials.

Dose : 10 to 40 mg/kg/day not exceeding 1000 mg is given as i.v. infusion in 200 mL of 5% dextrose over a period of 30 min and is repeated consecutively for 3 to 5 days. This is usually followed by oral prednisolone at a dose of 1mg/kg .

Cost : Inj (500 mg) Rs. 350.00 - 400.00

Cyclophosphamide

An alkylating agent used extensively as an anticancer drug is also widely used as an immunosuppressive drug in the treatment of immune mediated renal and rheumatic diseases. It acts by denaturing DNA and destroying rapidly multiplying immuno competent cells.

I: Primary glomerular diseases : Minimal change nephrotic syndrome, Crescentic glomerulonephritis.

In the former used as second line therapy for steroid sparing effect in steroid dependent state, frequent relapsers and secondary resistance to steroids. In the latter, it is used in combination with steroids for achieving better remission rates.

Secondary renal diseases : SLE with class IV lupus nephritis, Wegeners granulomatosis, microscopic polyarteritis, idiopathic crescentic GN and other vasculitidis with severe renal involvement.

C/I: Pregnancy, lactation, severe renal and hepatic failure, leucopenia, thrombocytopenia and dehydration.

P/C: Renal failure and dehydration. To be used in specialist care only.

S/E: Immediate side effects include bone marrow suppression, leukopaenia, agranulocytosis and serious infections, alopecia, oral ulcers, anaemia, GI disturbances, hyperemesis. Intravenous administration of large bolus doses can be associated with haemorrhagic cystitis due to its metabolite, acrolein. This can be prevented by concomitant administration of Mesna a thiol compound orally two hours prior to administration and ensuring adequate hydration and urine flow. Long term side effects include infertility especially in males, delayed puberty, and an increased risk of malignancy.

P/A: Tablet 50 mg

Injection i.v. 200 mg, 500 mg, 1 g.

Dose: Oral tablets : 2 -3 mg/kg/day for a period of 8 to 12 weeks. Cumulative total dose should not exceed 300 mg/kg .

Intravenous bolus infusions : 500 to 1000 mg given as infusion in 5% dextrose solution. Repeated every month for 6 to 12 months depending on severity and activity of disease.

This mode is preferred in patients with severe forms of renal disease.

D/I: Increased toxicity with cytotoxic drugs and allopurinol.

Cost :	Tab	50 mg	(10)	Rs. 80.00
	Inj	500 mg	(vial)	Rs. 70.00

Chlorambucil

Alkylating agent preferred by some due to its beneficial effects and relative safety.

12. Drugs Used in Diseases of Kidney and Urinary Tract

- I: Preferred immunosuppressive in membranous nephropathy. Alternated with oral prednisolone every 4 weeks for 6 months. Also useful in steroid resistant minimal change disease.

Dose : 0.1 to 0.3 mg /kg /day for 6 to 8 weeks in MCNS and alternate 4 weeks for 6 months in membranous nephropathy.

Cyclosporine

More specific immunosuppressive, widely used in transplantation to prevent rejection, is also used in certain primary glomerular diseases

- I: Steroid resistant minimal change disease, focal segmental glomerulosclerosis, membranous nephropathy and membrane proliferative GN.

C/A: Severe hypertension, severe renal and hepatic failure.

P/C: Monitor renal and hepatic function, monitor blood pressure and serum potassium. Caution in porphyria, hyperuricemia. To be used under specialist care only.

S/E: Dose dependant increase in urea and creatinine in early phase and chronic nephrotoxicity in prolonged use, hypertrichosis, tremor, hypertension, hepatic dysfunction, gingival hypertrophy, metabolic effects such as hyperkalemia, hypercholesterolemia, pancreatitis, convulsions, neuropathy, myopathy, haemolytic uremic syndrome, lymphoproliferative disorders.

P/A: Capsules 25, 50, 100 mg
Oral solution 100 mg/mL.

Dose : Renal transplantation 5 - 15 mg/kg in 2 divided doses initially, taper to 2 - 6 mg/kg maintenance.

Nephrotic syndrome 3 to 5 mg/kg/day for varying periods of time usually 3 months to 6 months.

D/I: Increased nephrotoxicity with NSAID and allopurinol, aminoglycosides and doxycycline.

Various antibacterial drugs and hypertensives alter cyclosporine levels in blood and thereby enhances toxicity or reduces effect. Cyclosporine has a narrow therapeutic window. ACE inhibitors and spironolactone increases risk of hyperkalemia.

Cost : Caps 25, 50, 100 mg (50) Rs. 1300.00, 2600.00, 5200.00 respectively.

Azathioprine

Purine antagonist, interferes with DNA synthesis, widely used in renal transplantation. Inferior to endoxan and chlorambucil in primary glomerular disease. Preferred immunosuppressive for class IV lupusnephritis. Less toxic than alkylating agents.

I: Lupus nephritis class III and IV, renal transplantation.

C/I: Hypersensitivity to mercaptopurine, allopurinol and azathioprine.

P/C: Monitoring of blood counts weekly for 8 weeks and thereafter every month. Reduce dose in hepatic and renal dysfunction and elderly. To be used under specialist care only.

S/E: Hypersensitivity reactions including deranged liver function, cholestatic jaundice, interstitial nephritis calls for permanent withdrawal. Dose related bonemarrow suppression, increased susceptibility to infections, pancreatitis, pneumonitis and alopecia.

P/A: Tablet 50 mg

Dose: 1-3 mg/kg/day

D/I: Increased toxicity with other cytotoxic drugs and allopurinol. Rifampicin reduces blood levels.

Cost : Tab 50 mg (10) Rs. 80.00

12.3 DRUG TREATMENT OF UROLITHIASIS

Stones in the urinary tract are composed of calcium oxalate, calcium phosphate, uric acid, triple phosphate (magnesium, ammonium phosphate) and cystine. Calcium stones account for 70 to 80% and triple phosphate 10-20% of all renal stones. Stones are formed when the concentration of the constituent substances in the urine exceeds the formation product (super saturation) or due to an imbalance between the promoters and inhibitors of stone formation. The predominant inhibitors are citrate, magnesium, pyrophosphates and certain glycopeptides in the urine.

General measures

If a single stone is found, after ruling out renal failure and UTI, dietary advice is given

1. Increase fluid intake to ensure at least 2 L of urine / day,
2. Reduce the protein intake to 1g/kg or less. Calcium intake in the range of 800-1000 mg / day.

Limit the salt intake to 100 mmol (5 g) or less.

3. He/she should be monitored annually to determine whether their stone disease is active. In a recurrent calcium stone former, rule out systemic and renal disease that can cause calculi.

When these dietary measures fail, pharmacological therapy is resorted to.

12.3.1 Drug therapy

Thiazide diuretics

Mechanism of action - Promote distal renal tubular calcium reabsorption, also increase proximal tubular reabsorption by ECF volume contraction.

I: Idiopathic hypercalciuria

Dose: Chlorthalidone : 25-50mg/day

12. Drugs Used in Diseases of Kidney and Urinary Tract

Hydrochlorothiazide : 25-100mg/day

Indapamide

A modified thiazide diuretic

Dose : 2.5mg/day

Potassium citrate

Mechanism of action – lowers urinary calcium excretion as well as increases urinary citrate excretion. Also alkalinises the urine.

I: Idiopathic hypercalciuria, idiopathic calcium stone formation, hypocitraturia, urate calculi, cystine stones, and prevention of growth of residual stone fragments after lithotripsy of struvite stones.

C/I:, P/C : Hyperkalemia and renal failure.

S/E: GI disturbances and hyperkalemia.

P/A: Powder 1 g = 14 mEq

Dose: 60-80 mEq/day

Allopurinol

Mechanism of action – Uric acid synthesis is reduced by inhibition of xanthine oxidase.

I: Primary and secondary hyperuricaemia, hyperuricosuria, gout, urate calculi.

S/E: Hypersensitivity reactions including fever, lymphadenopathy and eosinophilia and exfoliation resembling Steven Johnson Syndrome, leukopenia, leukocytosis, elevated aminotransferase levels and progressive renal insufficiency. Taste disturbances, vertigo, alopecia and neuropathy are other side effects.

P/A: Tablets 100 mg

Dose : 100 mg daily gradually increased to 300 mg daily over 3 weeks. Not to exceed 900 mg.

Cost : Tab 100 mg (10) Rs. 45.00

Pyridoxine

Mechanism of action – Pyridoxal phosphate (Vit B6) is a cofactor for the enzyme alanine glyoxalate transaminase

I: Primary hyper oxaluria, dietary hyper oxaluria.

P/A: Tablet 10 mg, 40 mg and 100 mg

Dose : Primary hyper oxaluria 100 - 1000 mg/day.

Dietary hyper oxaluria 25 - 100 mg/day.

Neutral phosphate

Mechanism of action – decrease in urinary calcium excretion, increase in

urinary pyrophosphate, and an increase in plasma phosphate which deregulates calcitrol production.

I: Idiopathic calcium stone former, idiopathic hypercalciuria

Orthophosphate

Mechanism of action – Reduction in urinary calcium excretion by unknown mechanism, and urinary pyrophosphate increases.

I: Primary hyper oxaluria, idiopathic calcium stone former used in combination with pyridoxine.

Dose : 30-40mg/kg/day.

Cholestyramine

Mechanism of action – binds oxalate in the lumen of the bowel

I: Enteric hypercalciuria

S/E: Steatorrhoea due to binding of bile salts, deficiency of fat soluble vitamins.

Dose : 4g q.d.s.

12.3.2 Chelating agents used in the treatment of cystine stones

Mechanism of action – increase cystine solubility

Penicillamine

S/E: Blood dyscrasias and nephropathy

Dose: 250mg of penicillamine can lower urine cystine by about 100mg

Captopril

Reduces cystine excretion by chelation. Rarely used for this indication

Dose : 75-100mg/day

Mercaptopropionyl glycine

Less toxic than penicillamine. Currently not available.

12.4 TREATMENT OF VOIDING DYSFUNCTION AND OTHER COMMON LOWER URINARY PROBLEMS

12.4.1 Drugs for Benign prostatic hypertrophy (BPH)

Alpha adrenergic blockers: These drugs relax the smooth muscles of the prostate and bladder outlet and increase urine flow.

Drugs used : Prazosin, Terazosin.

I: BHP gr I and II with post void residual urine volume less than 150 mL

C/I: Orthostatic hypotension, hypersensitivity.

12. Drugs Used in Diseases of Kidney and Urinary Tract

- P/C:** First dose effect may cause collapse, to be taken while retiring to bed.
- S/E:** Dizziness, hypotension, postural hypotension, drowsiness, headache, lethargy, dry mouth, urinary incontinence.
- Dose:** Prazosin : 0.5 mg daily for 3 to 5 days, then progressively increased to 2 mg b.d.
Terazosin : 1mg h.s daily to be increased to a maximum of 10 mg daily.

5-Alpha reductase inhibitor

Drugs used : Finasteride

Dose: 5 mg daily increased upto 20 mg daily.

12.4.2 Treatment of neurogenic voiding dysfunction

Parasympathomimetics

Improves voiding efficiency by increasing detrusor contraction. Useful in non obstructive neurogenic urinary retention.

Bethanechol, Carbachol, Distigmine.

- I:** Postoperative retention, neurogenic bladder (large capacity low pressure) sensory atonia
- CI:** Parkinsonism, myocardial infarction, bradycardia, arrhythmia, asthma, epilepsy, peptic ulcer, pregnancy, vagotonia.
- S/E:** Parasympathomimetic effects - nausea, vomiting, abdominal colic, blurred vision, bradycardia, sweating.
- P/A:** Tablets Bethanechol chloride 25 mg
- Dose:** Bethanechol : 10 to 25 mg t.d.s. to q.d.s. daily.
Carbachol: 2mg t.d.s. to q.d.s. daily
Distigmine : 5 mg daily
- Cost:** Tab Bethanechol chloride 25 mg(100) Rs 940.00

12.4.3 Drugs for urinary frequency and enuresis

Antimuscarinic drugs

Flavoxate

- I:** Urinary frequency, dysuria, urgency, incontinence, bladder spasms
- CI:** Intestinal obstruction, ulcerative colitis, megacolon, bladder neck obstruction, glaucoma, myasthenia.
- P/C:** Glaucoma, prostate hypertrophy, hiatus hernia with reflux oesophagitis.

S/E: Antimuscarinic effects as for atropine.

P/A: Tablet 200 mg

Dose: 200 mg t.d.s.

Cost : Tab 200 mg (10) Rs 72.00

Propanthelene Bromide

I: Adult enuresis

Dose : 15 to 30 mg b.d.or t.d.s.

12.4.4 Drugs used in Nocturnal enuresis

Drug therapy indicated only after 8 years if bladder training and conditioning fails.

Drugs used : **Desmopressin**

Tricyclics : amitriptylline and imipramine.

Miscellaneous drugs : **Oxybutinine**

Used in urinary incontinence, detrusor - sphincter dyssynergia

Dose: Adults : 5 mg b.d to t.d.s

Children < 5 years : 2.5 mg b.d.

12.4.5 Alkalinisation of urine

Decreases discomfort in cystitis, retards bacterial growth especially E.coli. Drugs used include -

Potassium citrate

P/C: Hyperkalemia

Dose: 3 g /6 h,

Sodium citrate

Dose: 2 g/8 h.

Sodium bicarbonate

Dose: 3 g/6 h.

Note : Sodium containing drugs are to be used with caution in patients with oedema and CCF. Potassium containing salts to be avoided in renal failure.

12.4.6 Acidification of urine

I: Infection by urease splitting organisms especially proteus, presence of stones, catheter induced mixed infections. Drug used include -

Ascorbic acid

Dose: 4 g daily in divided doses.

12.5 NEPHROTOXIC DRUGS

Kidneys are susceptible to drug toxicity since most of the drugs and their metabolites are excreted through kidneys and very high blood flow rate

12. Drugs Used in Diseases of Kidney and Urinary Tract

through kidney tissue increases drug delivery to kidneys. Large surfaces of the nephrons come in contact with the drugs. Moreover, some drugs are reabsorbed and excreted through tubular epithelial cells which in turn get damaged. Direct drug toxicity is also influenced by the concentration of the drug in the tubules due to reabsorption of water and the pH in the tubular lumen which influences precipitation of the drugs.

Drug Induced renal syndromes

1. Renal hypoperfusion – eg. NSAIDs, Cyclosporine, ACE Inhibitors
2. Glomerulopathy – Nephrotic syndrome : heavy metals – gold, antimony, mercury and platinum, penicillamine, captopril ; acute glomerulonephritis by rifampicin and penicillin.
3. Tubular injury :
ATN – eg. aminoglycosides, radiocontrast dyes, amphotericin - B

Isolated tubular syndromes:

Nephrogenic DI - lithium, demeclocycline, methoxyflurane

Hyperkalemia – NSAIDs, ACE Inhibitors, cyclosporin- A, beta-blockers, Potassium sparing diuretics

Hyponatremia – Diuretics, clofibrate, chlorpropamide, demeclocycline

4. Interstitial injury

Acute interstitial nephritis: penicillins, sulfa, rifampicin , allopurinol etc.

Chronic interstitial nephritis - cyclosporin-A, lithium, nitrosourea

5. Obstructive nephropathy

Retroperitoneal fibrosis: practalol, methesergide

Intrarenal obstruction: sulfa, quinolones.

6. Papillary necrosis – NSAIDs

7. Hypertension – cyclosporin A, steroids

12.5.1 Commonly encountered drug nephrotoxicity

I. Antibiotics

Aminoglycosides:

Incidence of acute renal insufficiency following treatment with aminoglycosides is 10-15%. Factors predisposing are - volume depletion, age, pre-existing renal disease, dose and duration of treatment, concomitant use of other nephrotoxic drugs. Nephrotoxicity is directly proportional to the amino residues - neomycin the most toxic and netilmycin least toxic.

Dose in renal insufficiency:- Loading dose unchanged; Interval extension methods preferred;

Drug dose = Normal dose \times $\frac{\text{Patients creatinine clearance}}{100}$

100

Amphotericin B

Incidence : 80-90% of patients who receive a full course

Prevention : Hydration, salt loading, Ca channel blockers and theophylline

Cephalosporins

Most toxic is cephalexin – dose >6g/day produces proximal convoluted tubules (PCT) necrosis and acute renal failure (ARF). Several of cephalosporins are reported to produce AIN. Dose modification is required only when GFR is <30mL/min. Third generation drugs least toxic.

Quinolones

Acute interstitial nephritis (AIN) with ARF – usually the duration of therapy is 3-21 days. Intratubular crystallization.

Incidence – low, mostly due to ciprofloxacin

Dose modification – only when GFR is below 25 mL.

Tetracyclines

Worsen azotemia and hyperkalemia – due to anti-anabolic effect.

Least toxic – doxycycline

Other tetracycline proximal tubular dysfunction and renal tubular acidosis (RTA).

Sulfonamides

Crystallization of drug in tubular and in parenchyma, acute interstitial nephritis (AIN), trimethoprim and pyrimethamine cause elevation in serum creatinine levels by competing with tubular secretion of creatinine. Dose is decreased to 50% when GFR <20mL/min

II. Radiocontrast media

Causes acute renal failure following i.v. administration of iodinated radiocontrast agents. Risk factors: Pre-existing renal disease, DM, multiple myeloma, older age, concomitant use of other nephrotoxic drugs. The presence of renal failure increases the risk of nephrotoxicity by 6-fold. The clinical presentation includes nonoliguric ARF with asymptomatic increases in serum creatinine. Most of the patients recover spontaneously with conservative treatment, with <10% of them requiring dialysis support. The incidence can be reduced by good hydration and prior use of diuretics and use of non-ionic low osmolar contrast agents.

III. Antiviral drugs

Acyclovir

• Usually causes tubule interstitial injury with crystallization in the distal tubule
Commonly produces nonoliguric renal failure within the first few days of therapy.

Ganciclovir Has got no nephrotoxic effects.

Foscarnet

Causes ATN of proximal tubular epithelial cells. Fluid and electrolyte abnormalities are frequent, especially hypocalcemia.

Zidovudine No nephrotoxic effects

IV. Anticancer drugs

Cisplatin

Commonly produces various types of electrolyte disturbances like hypomagnesemia, hypocalcemia and hypokalemia. Preventive measures include: infusion rate $<1\text{mg/kg}$, good hydration ($150\text{-}200\text{mL/h}$) during and 6 h after cisplatin administration; verapamil or captopril administration.

V. NSAIDs

The toxic effects are attributed to the inhibition of prostaglandin (PG) synthesis in the kidney which causes reversible deterioration of renal function. But they also cause acute interstitial nephritis (AIN), chronic interstitial nephritis (CIN), papillary necrosis. Some of them also cause glomerular lesions leading to nephrotic syndrome eg. fenoprofen. Because of PG synthesis inhibition, most of them produce sodium and water retention. Hyporeninemic hypoaldosteronism produces hyperkalemia. Long term use of NSAIDs causes analgesic nephropathy with chronic tubulo interstitial fibrosis. This is more common in females.

VI. Heavy metals

Lead : Acute lead nephropathy with damage to proximal tubule and Fanconi syndrome, occur in lead toxicity (Pb level $>100\text{mg/dL}$). Chronic exposure to lead leads to proteinuria, hyperuricemia, hypertension and chronic tubulo interstitial disease.

Mercury : The nephrotoxicity is mainly by mercury chloride. Acute poisoning with HgCl_2 produces proximal tubular necrosis and ARF.

Gold : The prevalences of proteinuria in therapeutic gold administration is 30%. The renal lesion is membranous nephropathy.

VII. ACE Inhibitors

Haemodynamic deterioration occur in the setting of bilateral RAS or unilateral stenosis in a solitary functioning kidney, may also occur in congestive cardiac failure (CCF), volume depletion and ADPKD. Other renal lesions described are membranous nephropathy, interstitial nephritis and acute tubular necrosis

VIII. Allergic interstitial nephritis

This is seen commonly with penicillins, sulfonamides, rifampicin, NSAIDs and others. It can occur with any drug other than those mentioned. It is to be differentiated from direct drug toxicity. Eosinophiluria is characteristic. This usually recovers on stopping the offending drug.

12.5.2 Drug dose modification in renal failure

I: Interval extension (in hours), D: Dose reduction method (percentage of normal dose) Unch:(unchanged)

	Method	GFR >50 mL/min	GFR 10-50 mL/min	GFR <10 mL/min
I. ANTIMICROBIALS				
Penicillin G	D	Unch.	75	25-50
Ampicillin	I	6	6-12	12-16
Amoxicillin	I	6	6-12	12-16
Cloxacillin	D	Unch.	Unch.	Unch.
Tetracycline	I	8-12	12-24	24
Doxycycline	I	12	12-18	18-24
Erythromycin	D	Unch.	Unch.	50-75
Metronidazole	D	Unch.	Unch.	50
Sulfamethoxazole	I	12	18	24
Trimethoprim	I	8-12	18	24
Vancomycin	I	24-72	72-240	240
Aminoglycosides				
Gentamicin	I	8-12	12	24-48
Amikacin	I	12-18	24-48	>48
Netilmicin	I	8-12	12	24-48
Quinolones				
Ciprofloxacin	D	Unch.	50-75	50
Norfloxacin	I	12	12-24	Avoid
Ofloxacin	D	Unch.	50	25-50
Pefloxacin	D	Unch.	Unch.	Unch.
Cephalosporins				
Cephazolin	I	8	12	24-48
1 st gen. Cephaloxins	I	6	6	8-12
gen. Cephadroxil	I	12	12-24	24-48
2 nd gen. Cefuroxime	D	45-100	10-45	5-10
Cefotaxime	I	Unch.	8-12	24
3 rd gen. Ceftriaxone	D	Unch.	Unch.	24
gen. Cefoperazone	I	Unch.	Unch.	Unch.
Ceftazidime	I	8-12	24-48	48-72
Anti tubercular drugs				
INH	I	8	8	8-12
Rifampicin	I	Unch.	Unch.	Unch.
Ethambutol	I	24	24-36	48
Pyrazinamide		Unch.	Unch.	Unch.
Antifungal agents				
Amphotericin B	I	24	24	24-36
Fluconazole	D	24	24-48	48-72
Ketoconazole	D	Unch.	Unch.	Unch.

12. Drugs Used in Diseases of Kidney and Urinary Tract

Antiviral

Acyclovir	I	Unch	24	48
Gancyclovir	I	12	24-48	48-96
Zidovudine	I	4	4	8

II ANALGESICS

Ketorolac	D	Unch.	50	50
All others – Normal dose				

III. ANTICOAGULANTS

Heparin	D	Unch.	Unch.	Unch.
Streptokinase	D	Unch.	Unch.	Unch.
Urokinase	D	Unch.	Unch.	Unch.
Warfarins	D	Unch.	Unch.	Unch.

IV. ANTIHYPERTENSIVES

Nifedipine	D	Unch.	Unch.	Unch.
Amlodipine	D	Unch.	Unch.	Unch.
Atenolol	I	24	48	96
Metoprolol	D	Unch.	Unch.	Unch.
2- methyl dopamine	I	6	9-18	12-24
Prazosin	D	Unch.	Unch.	Unch.
Clonidine	D	Unch.	Unch.	Unch.
Captopril	D	Unch	75	50
Enalapril	D	Unch.	75-100	50
Lisinopril	D	Unch.	50-75	25-50

V. CNS DRUGS

Alprazolam	D	Unch.	Unch.	Unch.
Amitryptilline	D	Unch.	Unch.	Unch.
Diazepam	D	Unch.	Unch.	Unch.
Clonazepam	D	Unch.	Unch.	Unch.
Haloperidol	D	Unch.	Unch.	Unch.
Chlorpromazine	D	Unch.	Unch.	Unch.
Phenobarbitone	D	Unch.	Unch.	Unch.
Phenytoin	D	Unch.	Unch.	Unch.
Sodium Valproate	D	Unch.	Unch.	Unch.

VI. ANTIDIABETIC DRUGS

Chlorpropamide	I	24	avoid	avoid
Glipizide	D	Unch.	Unch.	Unch.
Tolbutamide	D	Unch.	Unch.	Unch.

VII. MISCELLANEOUS

Allopurinol	I			8
12-24		48-72		
Lovastatin	D			Unch.
Unch.	Unch.			
Theophyllines	D			Unch.
Unch.	Unch.			

CHAPTER 13: ANAESTHETIC AGENTS

13.1 DRUGS USED FOR GENERAL ANAESTHESIA

13.1.1 Intravenous anaesthetics

Thiopentone sodium ★

This is a widely used intravenous anaesthetic agent. It has no analgesic properties and induction is rapid and smooth. The therapeutic margin is narrow with cardiovascular depression. Being alkaline it is highly irritant to the veins. Metabolism is slow and therefore sedative effects may persist for upto 24 hours. Repeated doses have cumulative effect.

I: Induction of general anaesthesia.

C/I: Avoid in porphyria, reduce the dose in liver diseases, elderly and the debilitated, hypovolemia.

P/C: Cross sensitivity or related problems, pregnancy, breast feeding.

S/E: Apnoea, allergic reactions, cardiac arrhythmia, respiratory depression, thrombophlebitis.

P/A: Injection 500 mg and 1 g vial.

Dose: 2.5 % or 5 % solution to be given i.v. Dosage is to be individualised - initially 100 - 150 mg over 10 - 15 seconds upto 4 mg / kg if required.

For children 6 - 7 mg / kg for induction.

D/I: Concurrent use of antihypertensive drugs result in an additive hypotensive effect. Ketamine and promethazine may increase the risk of hypotension.

Cost: Inj 1 g (vial) Rs. 44.00 - 45.00

Methohexitone sodium

Induction is less smooth, with greater incidence of hiccup. Recovery is rapid. Other features include tremor, involuntary movements, pain at injection site.

I: Induction and maintenance of anaesthesia for short procedures- for prolonged anaesthesia other agents may have to be employed

C/I: Porphyria ; in liver diseases dose has to be reduced

P/C: , D/I: Same as thiopentone sodium

S/E: As for thiopentone sodium. Abnormal muscle movements, coughing, sneezing, hiccup and laryngospasm occur more frequently than with thiopentone- sodium.

P/A: 100 mg in 10 mL vial. (powder for reconstitution)

500 mg in 50 mL vial.

Dose: Same as thiopentone sodium.

Cost: Not available in India.

Etomidate

This is an induction agent. Recovery is rapid without hangover effect. There is less of hypotension than with other agents and cause pain on injection. Involuntary muscle movements are a frequent occurrence and this may necessitate the administration of other drugs such as diazepam. Repeated doses cause adrenocortical suppression. Advantages include minimal cardiovascular disturbances, cerebral protection and only minimal respiratory depression.

I: Induction of anaesthesia.

C/I: Porphyria, reduce dose in liver diseases.

S/E: Adrenocortical suppression, pain on injection, thrombophlebitis, myoclonus, nausea and vomiting.

P/C: Pregnancy.

P/A: Etomidate - 2 mg/mL - 10 mL Amp. (In propylene glycol)

Dose: By slow i.v. 0.2 to 0.6 mg/kg for induction.

Maintenance dose - 10 mcg/kg/min infusion.

D/I: Same as thiopentone sodium

Cost: Not freely available in India.

Ketamine ✧

I: Induction and maintenance of anaesthesia, good analgesic property in subanaesthetic doses.

Maximum effect occurs within a few seconds. The muscle tone is increased, so also cardiovascular stimulation may occur. Recovery is relatively slow ($t_{1/2}$ 20-30 min). It causes bronchodilation, so ideal for bronchial asthma.

C/I: Hypertension, previous history of hallucination, psychiatric patients, coronary artery disease.

P/C: Avoid in those prone to hallucinations.

S/E: Respiratory secretions are mucous and therefore atropine may be required along with this drug. Hallucinations may occur, which are prevented by diazepam.

P/A: Ketamine hydrochloride

10 mg/mL 20 mL vial.

50 mg/mL 10 mL vial.

100 mg/mL 5 mL vial.

Dose: For short procedures, 6.5-13 mg/kg may be given i.m.; 10 mg/kg usually produces surgical anaesthesia for 12-25 min.

For diagnostic maneuvers and procedures not involving intense pain, the initial dose is 2mg/kg by slow i.v. injection over at least 60 seconds.

For short procedures, 1-4.5 mg/kg may be given i.v. 2mg/kg usually produces 5-10 min of surgical anaesthesia.

It can be given by i.v. infusion of a solution containing 1 mg/mL.

For longer procedures induction can be attained by a total dose of 0.5-2 mg/kg;

For maintenance 10- 45 mcg/kg/min can be given as a microdrip infusion, the rate being adjusted according to response.

D/I: Concurrent use with enflurane and halothane prolong the recovery from anaesthesia. Use of CNS depressing drugs lead to hypnosis. Interaction with thyroid hormones will lead to risk of hypertension and tachycardia.

Cost: Inj 50 mg/mL (10 mL) Rs. 66.00 - 104.00

Propofol

It is widely used. The recovery is rapid without hangover, but at times it may lead to pain at the site of injection. It is ideal for day care surgery.

I: Induction and maintenance of GA, sedation of ventilated patients receiving intensive care upto 3 days.

C/I: Propofol allergy.

P/C: Monitor blood lipid concentration in patients at risk of fat overload and bacterial contamination, while drawing up propofol emulsion.

S/E: Bradycardia, convulsions, anaphylaxis, delayed recovery from anaesthesia, hypotension, pain at site of injection.

P/A: Emulsion 10 mg/mL 20 mL Amp.

Injection 50 mL, 100 mL vial.

Prefilled syringes 50 mL

Dose: For induction it is given by i.v. 1-2.5 mg /kg at a rate of 20-40 mg every 10 seconds.

For maintenance, it is continued by i.v. infusion at the rate of 80-150 mcg/kg/min.

D/I: Alcohol and CNS depressant drugs produce hypotension.

Cost: Vial (20mL) Rs. 195.00

13.1.2 Inhalational agents

This includes volatile liquid anaesthetics and gaseous anaesthetics.

Volatile liquid anaesthetics include halothane, enflurane and isoflurane.

Indication: 1. Induction and maintenance of anaesthesia.

2. Sedation for short procedures.

Halothane ☆

Potent, smooth induction, non - irritant, pleasant vapour, seldom induce

conscious or breath - holding, widely used. MAC - 2.4

Induction and maintenance of anaesthesia. Used following induction with an intravenous agent.

C/I: Unexplained jaundice or fever, cardiorespiratory depression, concurrent use of adrenaline may precipitate ventricular arrhythmia. It produces moderate muscle relaxation.

P/C: In obstetrics it is to be used only in lightest plane. Adrenaline should be used only with caution.

In neurosurgery it is used with moderate hyperventilation. It has to be used with caution in compromised cardiac or liver function, early pregnancy and lactation.

S/E: Hepatotoxicity - previous exposure to halothane should be asked for in history. Repeated exposure is to be avoided within a period of 3 months. It may trigger malignant hyperthermia.

P/A: 250 mL bottle.

Dose: Adults - induction : dosage must be individualised.

Maintenance : inhalation 0.5 - 1.5 %,

Children : dosage must be individualised (2-4 % is needed).

D/I: Concurrent use with adrenaline increases the risk of adrenaline - induced ventricular arrhythmias and acute pulmonary oedema especially if hypoxia is present. Morphine enhances the respiratory depression caused by halothane. Chlorpromazine enhances depressant effect.

Cost: Liquid (250 mL) Rs. 1596.00 - 1597.00

Enflurane

It is less potent than halothane. It is a cardiorespiratory depressant. Ventricular arrhythmias are uncommon even when adrenaline is given concurrently. It causes EEG changes. It is to be avoided in epileptic patients. MAC - 1.68

I: Maintenance of anaesthesia.

C/I, P/C, D/I: Same as halothane

S/E: Triggers malignant hyperthermia.

P/A: 250 mL bottle.

Dose: Adults: Induction : dosage must be individualised

Maintenance : inhalation 0.5 - 3 %

Children : Dosage must be individualised.

Cost: Not freely available.

Isoflurane ☆

This is an isomer of enflurane, its potency is intermediate between halothane and enflurane. Risk of cardiac arrhythmias is less. Respiration is depressed. It produces muscle relaxation which is potentiated by other muscle

relaxant drugs. MAC - 1.15. It is ideal for neurosurgery with a reduction in intracranial pressure; maintains cerebral perfusion pressure. It is a potent vasodilator, therefore it can be used for producing induced hypotension. It may cause "coronary steal" in some patients.

I, C/I, P/C, D/I: Same as halothane

S/E: Trigger malignant hyperthermia. Since it is an irritant vapour it is less suitable for induction of anaesthesia especially in children.

P/A: Liquid 100 mL bottle.

Dose: Adults induction : inhalation 1.5-3%

maintenance: inhalation 1-3.5%

Children : dosage must be individualised.

Cost: Liquid 100 mL Rs. 1944.00 - 1945.00

13.1.3 Gaseous agents

Nitrous Oxide ☆

It is a good analgesic and a poor anaesthetic agent. MAC - 105.

I: Maintenance of anaesthesia (50 - 70 % in O₂), sub-anaesthetic concentration for analgesia.

C/I: Caution needed in the presence of air enclosing cavities, acute intestinal obstruction, pneumothorax

P/C: Pregnancy.

S/E: Deleterious effect in patients with air-containing closed space since it diffuses into such spaces with resulting increase in pressure. On prolonged use it may cause megaloblastic anaemia due to interference with Vit. B₁₂ metabolism. It may depress leucocyte function.

Dose: It is administered using a suitable anaesthetic apparatus as a mixture with 20-30 % Oxygen for maintenance of light anaesthesia.

D/I: Hypotensive effect occurs when used concurrently with any of the CNS depressant drugs.

13.1.4 Premedicants

Atropine ☆

This is an anticholinergic tertiary amine which crosses blood brain barrier

I: To prevent the formation of excess of bronchial and salivary secretions. It may be used with neostigmine to prevent bradycardia, excessive salivation and other muscarinic actions; to prevent bradycardia and hypotension associated with agents like halothane, propofol and suxamethonium; to prevent arrhythmias after myocardial infarction and CPR especially asystole.

C/I: Glaucoma, chronic respiratory disease, sick-sinus syndrome,

thyrotoxicoses, cardiac failure, pyloric stenosis, prostatic hypertrophy.

P/C: Elderly; urinary retention, prostatic enlargement, tachycardia, cardiac insufficiency, paralytic ileus, ulcerative colitis, and pyloric stenosis. It may aggravate gastro-oesophageal reflux, use with caution in pregnancy and breast feeding.

S/E: Tachycardia, central anticholinergic syndrome.

P/A: Injection : 1. 600 mcg/mL 1 mL ampoule
2. 100 mcg/mL - 5 mL, 10 mL, 30 mL disposable syringe
Drops 1%

Dose: For premedication, it is given by i.v., 300-600 mcg immediately before induction of anaesthesia, and in incremental doses of 100 mcg for the treatment of bradycardia. By i.m. the dose is 300-600 mcg, 30-60 minutes before induction. For children dose is 20 mcg / kg.

For control of muscarinic side effects of neostigmine during reversal of competitive neuromuscular block, it is given by i.v. in a dose of 0.6 -1.2 mg.

Total adult vagolytic dose - 3 mg.

D/I: Additive anticholinergic effect with quinidine and antidepressants..

Cost: Inj 0.6 mg/mL	(1 mL)	Rs. 3.00 - 4.00
Drops 1 %	(5 mL)	Rs. 10.00 - 11.00

Glycopyrronium Bromide (Glycopyrrolate)

It is a quaternary ammonium compound, does not cross blood brain barrier. It is a potent antisialagogue and has longer duration of action (approx. 6 hrs).

I., P/C, S/E : Same as atropine.

C/I: Glaucoma, obstructive uropathy, myasthenia gravis, severe ulcerative colitis.

P/A: Injection 200 mcg / mL, 1 mL amp, 3 mL amp.

Dose: For premedication it is given by i.m. or i.v. 10 mcg/kg, 200-400 mcg or 4-5 mcg/kg to a maximum of 400 mcg.

For children it is given by i.m. or i.v., 4-8 mcg/kg upto a maximum of 200 mcg.

For intraoperative use it is given by i.v. injection as for premedication.

For control of muscarinic side effects of neostigmine during reversal of competitive neuromuscular block it is given in a dose of 10 mcg / kg with 50 mcg/kg neostigmine.

D/I: Ventricular arrhythmias can occur on i.v. administration in presence of cyclopropane anaesthesia.

Cost: Inj 0.2 mg/mL	(10 x 1 mL)	Rs. 37.00 - 66.00
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Hyoscine Hydrobromide

- I: Drying secretions, producing amnesia and sedation. Therefore ideal as premedication in cardiac surgery.

C/I, P/C & D/I : Same as atropine.

S/E: Slows heart rate and so avoid in elderly.

P/A: Injection 0.4 mg/mL amp.

0.6 mg/mL amp.

Dose: Premedication, by s.c. or i.m., 200-600 mcg 30-60 min before induction of anaesthesia, usually with papaveretum

Children : 15 mcg/kg.

D/I: Its effect is potentiated by other anticholinergic drugs and tricyclic antidepressants. It delays the absorption of orally administered drugs.

13.1.5 Muscle relaxants

Atracurium Besylate ☆

- I: This is a non-depolarising muscle relaxant of intermediate duration and is widely used.

Histamine release may occur, related to total dose and speed of injection, which can be prevented by concurrent administration of H_1 and H_2 receptor blockers. This drug is non-cumulative. Metabolised by pH and temperature dependent Hoffman degradation, therefore ideal in hepatic and renal failure.

C/I: Hypersensitivity

P/C: Myasthenia gravis and other neuromuscular disorders, pregnancy, neonates, asthma.

S/E: Histamine release may occur, give rise to urticaria, laryngospasm and cause hypotension.

P/A: Injection 10 mg/mL - 2.5 mL, 5 mL, 10 mL ampoules.

Dose: By i.v. injection for adults and children over 1 month the initial dose is 300-600 mcg/kg.

Thereafter 100-200 mcg/kg is repeated as required.

By i.v. infusion, it can be given in a dose of 5-10 mcg/kg/min (300-600 mcg/kg/hour)

D/I: Quinidine and propranolol enhance the muscle relaxant effect.

Cost : Inj 10 mg/mL (2 mL) Rs. 83.00 - 84.00

Pancuronium Bromide ☆

- I: Non-depolarising muscle relaxant, long acting, produces moderate vagolytic action tachycardia and hypertension. So avoid in coronary artery disease.

- C/I: Hypersensitivity, anuria.
- P/C: Hepatic impairment, reduce dose in renal impairment.
- S/E: Itching of skin, excessive salivation, relatively low risk of side effects with histamine release.
- P/A: Injection pancuronium bromide 2 mg/mL - 2 mL amp.
- Dose: By i.v., initially for intubation 80-120 mcg/kg then 10-20 mcg/kg
Neonate; 30- 40 mcg/kg initially then 10-20 mcg/kg
Intensive care, by i.v., 60 mcg/kg every 1-11/2 h.
- D/I: Same as atracurium besylate
- Cost : Inj 2 mg/mL (2 mL) Rs. 16.00 - 17.00

Vecuronium Bromide

- I: Non-depolarising, intermediate duration, large doses may have cumulative effect, no histamine release, sympathetic blockade or vagolytic effect and it is ideal for cardiac surgery.
- C/I, S/E, D/I: Same as atracurium besylate
- P/C: Pregnancy, reduce dose in renal impairment and hepatic impairment.
- P/A: Powder for reconstitution - 4 mg/mL - 1 mL. Amp.
- Dose: By i.v. injection, initially 80-100 mcg/kg (maximum 250 mcg/kg), then 30- 50 mcg/kg as required;
By i.v. infusion, 50- 80 mcg/kg/h.
For children: as adult dose (onset more rapid).
- Cost : Inj 4 mg (1mL) Rs. 119.00- 120.00

Suxamethonium Chloride

- I: Depolarising muscle relaxant, short duration (5 min), rapid, complete, predictable paralysis, spontaneous recovery, action cannot be reversed with drugs.
- C/I: Hypersensitivity, severe liver disease, burns.
- P/C: The action cannot be reversed and clinical application is therefore limited.
- S/E: Prolonged muscle paralysis may occur in patients with low or atypical plasma pseudocholine esterase enzyme.
- P/A: Injection 50 mg/mL in 1 vial.
- Dose: By i.v. injection 600 mcg/kg (range 0.3-1.1 mg/kg depending on degree of relaxation required) usual range 20-100 mg
By i.v. infusion, as a 0.1% solution, 2-5 mg/min (2-5 mL/min)
By i.m. injection, adults and children, up to 2.5 mg/kg maximum 150 mg.

D/I: Arrhythmias develop if suxamethonium is given with digoxin.

Cyclophosphamide and thiotepa enhance the effect of suxamethonium.

Cost: Inj 50mg/mL (10 mL) Rs. 30.00

13.2 LOCAL ANAESTHETICS

Local Anaesthetics are drugs which are used as either injection or as application to mucous membrane to cause analgesia at particular regions. They block conduction along nerve fibres. The drugs differ in their duration of action, potency, toxicity, solubility and ability to penetrate nervous membranes. Their effectiveness also depends on the weight of the patient, age, clinical condition and degree of vascularity to the area under application. Various modes of applications are available including (a) topical (b) infiltration (c) epidural (d) spinal. The toxic effects include light headedness, sedation, gram oral paraesthesia, twitching and convulsion. To potentiate the effect of these drugs, adrenaline is added to produce local vasoconstriction and delay the absorption into the systemic circulation.

13.2.1 Sodium channel blockers

Lignocaine

I: Infiltration anaesthesia, dental anaesthesia, ventricular tachycardia or ectopics.

C/I: Hypovolemia, complete heart block.

P/C: Hepatic dysfunction, respiratory insufficiency impaired cardiac conduction, porphyria.

S/E: Mainly neurological - confusion, convulsion, higher doses may produce CVS collapse.

P/A: Injection 0.5% , 1% and 2 %

Combination with adrenaline 1/200000 (5 mcg/mL)

Cream 2.5%

Jet Spray 4%

Spray 10%

Dose: Surface anaesthesia. 2-4 %

Maximum dose : 3 mg/kg (without adrenaline)

7 mg/kg (with adrenaline)

Infiltration anaesthesia - Maximum 200mg.

Bupivacaine

Has a longer duration of action, slower onset of action. It is more cardiotoxic compared to lignocaine.

I: Local infiltration, peripheral nerve block, epidural block.

C/I:, P/C : S/E : Similar to lignocaine

P/A: Injection 2.5 mg/mL, 5 mg/mL

Dose:	Local infiltration	0.25% (upto 60 mL)
	Peripheral nerve block	0.25%
	Epidural block	0.5 - 0.75%
	Maximum dose :	2 mg/kg (with or without adrenaline)

Prilocaine

I: Infiltration, intravenous regional anaesthesia, nerve block, dental anaesthesia

C/I: P/C: S/E : Same as lignocaine and methaemoglobinemia.

Dose:	Injection	0.5% - (5 mg/mL)
		1% - (10 mg/mL)
		2% - (20 mg/mL)
		4% - (40 mg/mL)

Procaine

Shorter duration of action compared to lignocaine. Not useful as surface anaesthetic

I: Infiltration and regional routes

C/I: P/C: S/E : Same as lignocaine

P/A:	0.5%	(200 mL)
	1 %	(100 mL) with adrenaline

Amethocaine

Potent topical anaesthetic agent should never be applied on inflamed or highly vascular surfaces.

I: Topical local anaesthetic drug

S/E: Oedema, pruritus, erythema

Dose : 4% gel. (not recommended in infants)

Ropivacaine

Long acting similar to bupivacaine but less cardiotoxic.

I: Infiltration anaesthesia, epidural anaesthesia.

C/I: P/C: S/E : Same as lignocaine

Dose: 2 mg/mL.

13.2.2 Miscellaneous local anaesthetics**Chlorprocaine**

It is a short acting local anaesthetic.

Benzocaine**Mepivacaine**

CHAPTER 14: DRUGS USED IN DERMATOLOGY

Dermatology mainly deals with the problems of the skin, mucous membrane and their appendages. Next to muscle and bone, skin is the largest organ. Though the vast majority of dermatological lesions appear to be superficial, many of them have systemic counterparts. For example, superficial rash may be representing a major complaint in diseases like secondary syphilis, lupus erythematosus or immunodeficiency. So also a purely initial dermatological lesion may give rise to severe systemic complications. For example, streptococci infection of scabies may give rise to glomerulonephritis. Psoriasis which starts as a cutaneous lesion may be associated with arthropathy. Drugs used for topical application in skin and mucous membrane lesions, if used indiscriminately, may give rise to systemic complications. For example, corticosteroids, oestrogens, etc. Several drugs administered for various conditions give rise to cutaneous manifestations such as rashes, bullae, fixed drug eruptions, exfoliative dermatitis and Stevens Johnson's syndrome. Many infections start with skin manifestation as their major presenting symptoms. Example chicken pox, measles, german measles. Therefore, it is very important that the physician considers all dermatological problems as having very close interrelationship with several systems in the body. Therefore treatment of several dermatological disorders involves topical use of drugs as well as systemic use. It should also be remembered that many of the preparations containing antibiotics and other chemicals cause sensitization to the drug as well as confer resistance to the infecting microbe. Since many dermatological preparations are available as over the counter (OTC) drugs, there is a great chance for their misuse and the secondary ill-effects caused by them. It is therefore important that the physician limits their use to the minimum and also use the appropriate drug. Educating the public against self medication and on the ill-effects of OTC drugs should also be undertaken.

Since most of the drugs used in systemic therapy have been included in other sections, they are only indicated. The reader is directed to refer to their main description in the text. Topically used drugs are described in detail.

14.1 SUPERFICIAL BACTERIAL INFECTIONS

These include pyoderma, ecthyma, cellulitis, folliculitis, furuncles.

14.1.1 Topical therapy

Mupirocin

- I: Primary and secondary skin infections
- C/I: Known hypersensitivity to the drug.
- P/C : Avoid contact with the eyes. Moderate to severe renal impairment
Avoid prolonged use. Don't mix with other preparations.
- S/E: Itching, burning, erythema, stinging and dryness, cutaneous sensitization reactions.

Fusidic Acid

- I: Primary and Secondary pyodermas caused by gram positive organisms.
- C/I: Known hypersensitivity.
- S/E: Hypersensitivity reactions.

Sisomycin

- I: Primary and secondary skin infection.
- C/I: Hypersensitivity to aminoglycoside antibiotics.
- P/C: Renal impairment
- S/E: Ototoxicity, nephrotoxicity, tinnitus, vertigo, ataxia, tremor, azotaemia.
- P/A: Injection 10 mg, 50 mg
- Dose: Adult - 7.5 mg/kg/day 8 h, i.m. or i.v.
Children - 3 mg/kg/day 8 h, i.m. or i.v.
- D/I: Aminoglycosides potentiates ototoxicity and nephrotoxicity. Vancomycin and cephalosporins potentiates nephrotoxicity. Ethacrynic acid potentiates ototoxicity. Absorption of betalactum antibiotics decreased.
- Cost: Inj 10 mg (1 mL) Rs. 9.00 - 14.00

Neomycin + Bacitracin + Polymyxin

- I: Any external infection.
- C/I: Pre-existing nerve deafness, preterm infants.
- P/C: Renal impairment, large areas of skin damage.
- S/E: Hypersensitivity reactions.
- P/A: Ointment (Polymixin 5000 units + neomycin 3400 units + bacitracin 400 units)
Powder (Polymixin 5000 units + neomycin 3400 units + bacitracin 400 units)
- Dose: Sprinkle or apply over infected area 2 - 4 times daily.
- D/I: Potentiates aminoglycoside nephrotoxicity, neuromuscular blockade potentiated by sedatives, muscle relaxants and aminoglycosides. Synergy with trimethoprim and rifampicin.
- Cost: Ointment (Polymixin 5000 units + neomycin 3400 units + bacitracin 400 units) 15 g Rs. 18.00 - 20.00
Powder (Polymixin 5000 units + neomycin 3400 units + bacitracin 400 units) 10 g Rs. 16.00 - 18.00

Framycetin Sulphate

- I: Skin infection, otitis externa, burns and scalds, ophthalmic infections.

- C/I: Viral and tuberculous infections, varicella, vaccinia.
P/C : Known hypersensitivity to aminoglycoside antibiotics.
S/E: Rare.
P/A: Eye ointment 0.5 % w/w
Eye drops 0.5 w/w.
Impregnated gauze 1 %
Cream 0.5 % w/w.
Dose : Frequent local application for few days.
D/I: None reported.
Cost : Not freely available.

Clindamycin

- I: Bacterial skin infection especially Staphylococcal.

14.1.2 Systemic therapy

Tetracycline

- I: Common bacterial skin infections, chlamydial infections - urethritis, pelvic inflammatory disease, and lymphogranuloma venereum, syphilis, granuloma inguinale, chancroid, yaws, nocardia infection, acne, rosacea, perioral dermatitis.
C/I: Pregnant women, children under the age of 8.
P/C : Concurrent use of barbiturates, phenytoin, carbamazepine, ketoconazole, digoxin.
S/E: Gastric intolerance, pseudomembranous colitis, urticaria, phototoxic dermatitis, photoonycholysis, fixed drug eruptions, renal and hepatotoxicity, pseudotumour cerebri.

Minocycline

- I: Bacterial skin infections, acne, rosacea, Hansen's disease, UTI, chancroid, gonorrhoea, skin and soft tissue infections.
C/I, P/C :, D/I : Same as for tetracycline.
S/E: Gastritis, pigmentation, phototoxicity, greyish discoloration of teeth, black thyroid glands, black galactorrhoea, dizziness, vertigo, ataxia
P/A: Tablet 50 mg, 100 mg
Capsules 50 mg, 100 mg.
Injection 100 mg vial
Suspension 50 mg/5 mL
Dose : 100 mg b.d. for 10- 20 days, oral.
Cost : Caps 50 mg (6) Rs. 47.00 - 50.00
Other preparations are not freely available.

Erythromycin

- I: Skin and soft tissue infections caused by streptococci and staphylococcus, chlamydia trachomatis, reithritis, erythrasma, syphilis, gonorrhoea, chancroid, granuloma inguinale, lyme disease.
- C/I: Hypersensitivity, pregnancy.
- P/C: Concurrent administration of theophylline, cyclosporine, carbamazepine, digoxin etc.
- S/E: Gastric intolerance, cholestatic jaundice, pseudomembraneous colitis.

Penicillins (crystalline and procaine penicillin)

- I: Syphilis, gonorrhoea, skin and soft tissue infections caused by streptococcus and staphylococcus, gram negative skin infections, bacterial vaginosis, lyme disease.
- C/I: Hypersensitivity, cross hypersensitivity to cephalosporins.
- P/C: Anaphylactic reactions, drug interactions with erythromycin and tetracycline.
- S/E: Urticaria, anaphylaxis, morbilliform drug eruption, exfoliative dermatitis, serum sickness, Stevens -Johnson's syndrome, Jamisch - Herxheimer reaction, pseudomembraneous colitis.

Cephalosporins

- I: Skin and soft tissue infections caused by gram positive and negative bacteria, gonorrhoea, lyme disease.
- C/I: Known hypersensitivity to cephalosporins or Penicillins.
- S/E: Maculopapular rashes, eosinophilia, drug fever, urticaria, anaphylaxis, GIT disturbances, pseudomembraneous colitis.

Amoxycillin

- I: Skin and soft tissue infections caused by gram positive and negative bacteria, gonorrhoea, chancroid
- C/I: Known hypersensitivity.
- S/E: GI disturbances, candidal overgrowth, dizziness, urticaria, fever and mild hepatic and renal toxicity.

Trimethoprim - Sulfamethoxazole

- I: Gonorrhoea, non-gonococcal urethritis, chancroid, lymphogranuloma venereum, common skin infections by bacteria nocardia and mycobacterium marinum, brucellosis, melioidosis, hidradenitis suppurativa.
- C/I: Severe liver and haematologic disease, G6PD deficiency, folate deficiency.
- P/C: Simultaneous use of other antifolate drugs, anticoagulants, phenytoin, sulfonyleurea, methotrexate, thiazide diuretics and cyclosporine.
- S/E: GI upset, erythematous maculopapular eruption, urticaria, Stevens

Johnson's syndrome, phototoxicity, leucopenia, thrombocytopenia, haemolytic anaemia.

Rifampicin

- I: Hansen's disease, staphylococcal skin infection, chancroid, lymphogranuloma venerum, gonorrhoea, chlamydial urethritis, leishmaniasis, cutaneous tuberculosis.
- C/I: Pregnancy, known hypersensitivity, impaired liver function.
- P/C: Simultaneous use of other hepatotoxic drugs, PAS, INH, ketoconazole, digoxin, oral contraceptives, etc.
- S/E: Red discolouration of urine and tears, hypersensitivity, pemphigus, pseudomembranous colitis, thrombocytopenia purpura, haemolytic anaemia, renal failure.

Ciprofloxacin

- I: Primary and secondary pyoderma caused by gram positive and negative bacteria, gonorrhoea, non-gonococcal urethritis, chancroid.
- C/I: Pregnancy, childhood, lactation, known hypersensitivity to quinolones.
- P/C: Cross - allergensitivity to penicillin and cephalosporins, simultaneous use of theophylline, cyclosporine and antacids.
- S/E: GI disturbances, headache, arthritis, elevation of liver enzymes, eosinophilia, crystalluria.

Other Quinolone Drugs - ofloxacin, lomefloxacin, sparfloxacin

- I: Hansen's disease - primary and secondary pyoderma.
- C/I : , P/C : , S/E : , D/I : Same as ciprofloxacin.

Metronidazole

- I: Cutaneous infection by bacteroides, B. fragilis, clostridium, peptococcus and fusobacterium species, trichomoniasis, bacterial vaginitis.
- C/I: Severe hypersensitivity reaction, pregnancy.
- P/C: Liver disease, history of seizures, simultaneous use of alcohol, anticoagulants, cimetidine, phenobarbitone and phenytoin
- S/E: GI upset, headache, ataxia, peripheral neuropathy, pseudomembranous colitis.

Azithromycin and Roxithromycin

- I: Skin and soft tissue bacterial infection, gonococcal and non-gonococcal urethritis.
- C/I: Hepatic impairment
- P/C: Renal or hepatic disorders, pregnancy, lactation, heart diseases, simultaneous use of antacids, digoxin, cyclosporine, anticoagulants and antihistamine.

S/E: Gastritis, transient elevation of liver enzymes, allergic skin rashes, angioedema, cholestatic jaundice, pseudomembranous colitis.

Clarithromycin

I: Skin and soft tissue bacterial infection, Hansen's disease.

C/I: Hypersensitivity to macrolides, history of jaundice.

P/C: Cholestatic jaundice, abnormal liver function test, pregnancy, lactation.

S/E: GI disturbances, allergic reactions.

14.2 SUPERFICIAL AND DEEP MYCOSES

14.2.1 Topical therapy

Amphotericin-B

I: Superficial candida albicans infection.

Ciclopirox

I: Candidiasis, dermatophytosis, pityrosporum infections, onychomycosis.

C/I: Hypersensitivity

P/C: Use light fitting under garments especially made of cotton. In case of toe infection use well ventilated shoes or sandals. Using a bland absorbent powder or antifungal powder on skin is advised.

S/E: Burning, itching, redness, swelling.

P/A: Cream 1 % w/w

Lotion 1 % w/w

Dose: Topical application to skin and surrounding area 2 times daily.

D/I: None reported.

Cost: Not freely available.

Econazole

I: Dermatophytosis, candidiasis - cutaneous and vaginal.

C/I: Hypersensitivity.

P/C: With caution in intravaginal use, pregnancy and lactation.

S/E: Local irritation and sensitization on topical use.

P/A: Pessary 150 mg

Cream 1 % w/w

Dose: Cream: Apply 3 times daily for 2 - 4 weeks.

Pessary: 1 tab intravaginally h.s. for 3 days.

D/I: Antagonises polyene antibiotics.

Cost : Pessary 150 mg (3) Rs. 55.00 - 58.00
Cream 1 % w/w (15 g) Rs. 25.00 - 30.00

Haloprogin

I: Dermatophytosis, candidiasis, tinea infection and pityriasis, versicolor.
S/E: Irritation, pruritus, vesiculation. Increased maceration and exacerbation of existing lesions.
P/A: Lotion 1 %
Cream 1 %
Cost : Not freely available.

Ketoconazole (see section 2.3.1, III)

I: Dermatophytosis, pityrosporum infection, seborrheic dermatitis.
C/I: Hypersensitivity
S/E: Skin irritation.

Naftifine

I: Dermatophytosis, candidiasis
C/I: Hypersensitivity, pregnancy, lactation.
P/C: Avoid contact with eyes and mucous membrane, avoid use of occlusive dressing on area being treated, use well ventilated sandals and loose fitting cotton under garments. Simultaneous use of antifungal powder is also advised.
S/E: Dry skin, itching, redness, burning or stinging.
P/A: Cream 1 % w/w
Lotion 1 % w/w
Dose : Local application 1 - 2 times daily.
Cost : Not freely available.

Oxiconazole

I: Dermatophytosis
C/I: Hypersensitivity, lactation.
P/C: Avoid contact with eyes, do not use intra vaginally. Same as that of econazole
S/E: Local irritation - burning, itching, stinging, redness.
P/A: Cream 1 % w/w
Lotion 1 % w/w
Dose : Local application 1 - 2 times daily.
Cost : Not freely available.

Sulconazole

- I: Dermatophytosis, tinea versicolor.
- C/I: Hypersensitivity to the drug or other imidazole antifungals.
- P/C: Avoid contact with eyes, avoid occlusive dressing over the medication. Same as for econazole.
- S/E: Burning, stinging, itching, redness of skin.
- P/A: Cream 1 % w/w
Lotion 1 % w/w
- Dose: Local application 1 - 2 times daily.
- D/I: None reported.
- Cost: Not freely available.

Terbinafine (see section 2.3.1, V)

- I: Dermatophytosis.

Thymol

- I: Candidiasis
- C/I: Hypersensitivity.
- P/C: Irritant to gastric mucosa.
- S/E: Rashes.
- P/A: Compound thymol glycerin gargle / mouth wash (50 mg thymol)
Thymol mouth wash compound (150 mg thymol)
- Dose: Dilute 4 - 7 times and use as mouth wash/gargle.
- D/I: Fats and alcohol increase absorption and aggravate toxic symptoms.
- Cost: Not freely available.

Whitfield's Ointment

(Benzoic acid 6% and salicylic acid 3% in emulsifying ointment)

- I: Dermatophytosis.
- C/I: Hypersensitivity.
- P/C: Avoid contact with eyes and mucous membrane.
- S/E: Irritant to eye, skin and mucous membrane.
- P/A: Ointment
- Dose: Local application 2 - 3 times daily.
- D/I: Activity reduced in presence of non-ionic surfactants, reduced activity in presence of ferric salts and salts of heavy metals.
- Cost: Ointment (20 g) Rs. 9.00 - 10.00

Castellani's Paint

(Magenta 400 mg, boric acid 800 mg, phenol 4 g, resorcinol 8g, acetone 4 mL, 90% alcohol 8.5 mL, water to 100 mL)

I: Bacterial and fungal infection of skin, intestigenous inflammation.

C/I: Hypersensitivity.

P/C : Increased risk of tumour while handling.

S/E: Methemoglobinaemia.

P/A: Paint

Dose : For local application as directed by physician.

D/I: None reported

Cost : Not freely available.

Clotrimazole (see section 2.3.1, III)

I: Dermatophytosis, candidiasis, trichomoniasis

Miconazole (see section 2.3.1, III)

I: Dermatophytosis, candidiasis

Gentian Violet

I: Candidiasis, Vincent's angina, dermatophytosis, secondary bacterial infection.

C/I: Hypersensitivity, porphyria

P/C : Avoid contact with eyes.

S/E: Nausea, vomiting, diarrhoea, abdominal pain, ulceration of mucous membrane.

P/A: Cream 1.2 - 1.6 %

Topical solution 0.95 - 1.05 %

Dose : For local application only.

D/I: None reported.

Cost : Solution (15 mL) Rs. 5.00 - 6.00

Sodium Thiosulphate

I: Extensive tinea versicolor, pityriasis versicolor.

S/E: Osmotic disturbances, large oral dose cause catharsis.

P/A: Lotion 20 % w/w

Dose : For local application.

Cost : Not freely available.

Tolnaftate (see section 2.3.1, IV)

I: Dermatophytosis, Tinea versicular.

Undecenoic acid

I: Dermatophytosis.

S/E: Irritation

P/A: Compound undecylenic acid ointment.

Zinc undecenoate dusting powder.

Dose: For local application.

Cost: Not freely available.

14.2.2 Systemic therapy

Fluconazole (see section 2.3.1, III)

I: Systemic candidiasis, cryptococcosis, other subcutaneous and deep mycoses, dermatophytosis of skin, nails and hair, tinea versicolor.

Itraconazole (see section 2.3.1, III)

I: Same as for fluconazole.

Ketoconazole (see section 2.3.1, III)

I: Candidiasis, Blastomycosis, Chromomycosis, dermatophytosis, tinea versicolor, pityrosporum folliculitis, seborrheic dermatitis, psoriasis of scalp.

Giriseofulvin (see section 2.3.1, I B)

I: Dermatophytosis of skin, nails and hair, lichen planus.

C/I: Hypersensitivity, porphyria, hepatocellular failure, pregnancy.

P/C: Simultaneous use of anticoagulants and phenobarbitone.

S/E: Urticaria fixed drug eruption, phototoxicity, exfoliative dermatitis, hepatotoxicity, leucopenia.

Terbinafine (see section 2.3.1, V)

I: Candidiasis, dermatophytosis.

S/E: Gastric intolerance, vomiting, diarrhoea, headache, erectile dysfunction.

Flucytosine

I: Systemic candidiasis, cryptococcosis, aspergillosis

Nystatin (see section 2.3.1, I A)

I: Cutaneous and mucos membrane candidiasis, seborrheic dermatosis, acne vulgaris.

Amphotericin - B (see section 2.3.1, I A)

I: Oral and oesophageal candidiasis. cryptococcal meningitis, histoplasmosis, coccidioidomycosis

14.3 VIRAL INFECTION

14.3.1 Warts

Topical therapy

1. Salicylic acid (5 - 20 %)
2. Lactic acid (5 - 10 %)
3. Cantharidin
4. Podophyllum resin (25% in tincture benzoin).
5. Trichloroacetic acid (50 - 80 %)
6. Monochloroacetic acid (80%)
7. Phenol

14.3.2 Molluscum contagiosum

Topical therapy

1. Phenol
2. Trichloroacetic acid (50 - 80%)
3. Cantharidin
4. Tretinoin
5. 5 - fluorouracil.

14.3.3 Herpes simplex

Topical therapy

1. Idoxuridine (IDUR)
2. Adenosine arabinoside
3. Acyclovir
4. Dimethyl Sulfoxide (DMSO)

14.3.4 Herpes genitalis

Topical therapy - As for Herpes simplex

Systemic therapy - Acyclovir, Ganciclovir, Foscarnet

Acyclovir

I: Herpes genitalis - primary and recurrent, mucocutaneous HSV infection in the immunocompromised, recurrent erythema multiforme, eczema herpetum, varicella in the immunocompromised. Herpes zoster, AIDS (along with AZT).

C/I: Hypersensitivity.

P/C: Simultaneous use of Amphotericin - B, Ketoconazole.

S/E: Renal toxicity, nausea, vomiting, diarrhoea, headache, vertigo, dizziness, ataxia, anorexia, tremors and seizures.

Ganciclovir

I: Herpes simplex virus infection, cytomegalovirus(CMV) infection in HIV infected patient.

C/I: Known hypersensitivity.

P/C: Impaired renal function, monitoring of blood count during therapy, concomitant administration of other myelosuppressive drugs.

S/E: Anaemia, leucopenia, thrombocytopenia, fever, rash, abnormal liver function test, behavioural changes, psychosis convulsions and coma.

Foscarnet (see section 2.4.1, I)

14.3.5 Herpes zoster (see section 2.4.1, I)

1. Acyclovir (see section 2.4.1, I)

2. Ganciclovir (see section 2.4.1, I)

3. Foscarnet (see section 2.4.1, I)

14.4 PSORIASIS

14.4.1 Local therapy

Emollients

Liquid paraffin

White soft paraffin

I: Acute cases of psoriasis

Ichthyosis - primary and secondary

C/I: Acute oozing lesion.

P/C: Hot humid condition.

S/E: Folliculitis.

P/A: Liquid paraffin (100 mL, 400 mL)

Cost : Liquid paraffin (100 mL) Rs. 23.00 - 25.00

Salicylic acid

I: Psoriasis, verrucae vulgaris, dermatosis with dry keratotic lesion, onychomycosis, acne, warts

C/I: Acute cases of Psoriasis, guttate psoriasis

P/C: Avoid contact with eyes and mucous membrane, inflamed skin, avoid simultaneous use with other topical skin medications and cosmetics.

S/E: Local irritation, pustulation, exfoliable dermatitis.

P/A: Collodion 10%

Cream 2%

Lotion 2%

Ointment 2%

D/I: Concurrent use of salicylic acid with preparations containing benzoyl peroxide, resorcinol, sulphur, tretinoin, or acne preparations, or alcohol containing preparations like cosmetics and toiletries may cause a cumulative irritant or drying effect and resulting in excessive irritation of the skin.

Coal Tar Ointment

I: Psoriasis, Atopic dermatitis.

C/I: Acute onset psoriasis, guttate, pustular and erythrodermic psoriasis.

P/C: Long term use may be carcinogenic, may cause acne or lesions.

S/E: Irritation, folliculitis.

P/A: Ointment 1% w/w

Soap

D/I: Concurrent use with photosensitizing medications can cause additive photosensitizing effects; concurrent use with topical or systemic methoxsalen is not recommended.

Cost : Oint 1%w/w (15 g) Rs. 18.00 - 20.00

Soap (1) Rs. 18.00 - 20.00

Dithranol paste

I: Psoriasis

C/I: Same as for coal tar.

P/C: Do not use on inflamed skin, irritant to eye and mucous membrane

S/E: Irritation, staining, folliculitis.

P/A: Cream 0.5 %, 1%

Ointment 0.4 %, 1 %, 2%

Paste 1 %

D/I: Concurrent use with photosensitizing medications can cause additive photosensitizing effects.

Cost : Ointment 1 % (25 g) Rs. 15.00 - 20.00

Topical Steroids

I: Inflammatory condition of skin and mucous membrane.

C/I: Primary bacterial or viral infection, wounds and ulcers.

P/C: Long term use especially on soft skin.

S/E: Atrophy, stiae, telangiectasia, bacterial and fungal super infections, systemic absorption and toxicity if applied on extensive areas.

Topical Vitamin D Analogues

Calcitriol (see section 4.2.1)

Calipotriol

I: Psoriasis.

C/I: Hypercalcemia, hypercalciuria, hypervitaminosis D, nephrolithiasis, severe extensive psoriasis, pregnancy, children.

P/C: Avoid use on face and exposure to sunlight

S/E: Photosensitivity, local irritation.

P/A: Ointment 0.005 %w/w

Dose: As directed by physician

D/I: None reported

Cost: Ointment 0.005 %w/w (30 g) Rs. 695.00 - 700.00

14.4.2 Systemic therapy

Psoralen with UVA therapy (PUVA)

I: Psoriasis, vitiligo, mycosis fungoides, atopic dermatitis, lichen planus, parapsoriasis, pruritis of HIV, prunigo modularis, granuloma annulare, sescoidosis, mastocytosis, alopecia areata, GVHD.

C/I: Photosensitive diseases, hypersensitivity to psoralen melanoma or history of melanoma, extensive cutaneous squamous cell carcinoma, aphakia, pregnancy and lactation, severe cardiac and hepatic disorders, patients below the age of 12 years.

P/C: Use with caution in hepatic insufficiency, cardiac diseases, increased risk of cataract with PUVA therapy. Increased risk of carcinoma and skin burns. Provide eye and skin sun protection.

S/E: Acute - erythema, pruritis, nausea, headache, photosensitivity.

Chronic - cataract, photokeratoconjunctivitis, cutaneous carcinomas, freckling, increased contact allergy, bullous pemphigoid, lupus erythematosus, hepatotoxicity, leukaemia, nephrotic syndrome.

P/A: Tablet 5 mg, 10 mg

Ointment 10 mg/g

Lotion 25 mg/15 mL

Dose: 0.6-0.7 mg/kg bw daily, oral

D/I: Any drug that increases the sensitivity of the skin may increase the risk of redness, blistering, peeling, e.g., griseofulvin, thiazide diuretics, phenothiazines, sulfonamides and tetracyclines

Cost: Tablet 10 mg (40) Rs. 28.00-30.00

Ointment 10 mg/g (30 g) Rs. 23.00-25.00

Lotion 25 mg/15 mL (15 mL) Rs. 17.00-18.00

Methotrexate

I: Psoriasis, mycosis fungoides, pityriasis rubrapilaris, Reiter's disease,

pemphigus, bullous pemphigoid, dermatomyonitis, lupus erythematosus, sarcoidosis, keloids, lymphomatoid papulosis.

C/I: Pregnancy and lactation, decreased renal function, hepatic diseases, severe haematological abnormalities, alcoholism, active infectious diseases, immuno deficiency, unreliable patients

P/C : Assessment of liver functions, renal function, blood count, pulmonary functions, concurrent administration of protein binding drugs.

S/E: Hepatotoxicity, pulmonary toxicity, bone marrow suppression, gastric intolerance, sterility, renal toxicity.

Retinoids (Isotretinoin, Etretnate and Acitretin)

I: Severe forms of psoriasis, severe recalcitrant acne, premalignant skin conditions, squamous cell carcinoma, melanoma, mycosis ferryoides, lupus errythematosus, Danier's disease.

C/I: Pregnancy, hypersensitivity, hyperlipidemia, hepatic dysfunction, hypervitaminosis A, hepatic / renal impairment, acute eczema and dermatitis, rosacea, children.

P/C : Avoid contact with eyes and mucous membrane, avoid concomittant conventional acne treatment, avoid UV and sunlight.

S/E: Hepatotoxicity, teratogenicity, hyperlipidemia, ocular toxicity, pseudotumour cerebri, bone changes, photosensitivity, itching, redness, peeling, xerosis of skin.

P/A: Isotretinoin Cream 0.025 %, 0.05 %
 Capsules 10 mg, 20 mg, 40 mg
Etretnate Capsule 10 mg, 25 mg

Acitretin is an active metabolite of Etretnate

Dose : Isotretinoin - Local application for 1-2 times daily

Etretnate - 0.75 mg/kg/day in divided doses for 2-4 weeks, reduced to 0.5 mg/kg/day in divided doses for further 6-8 weeks

D/I: Excessive irritation of the skin with cosmetics, alcohol consumption increases plasma triglyceride concentration, additive toxic effect with Vitamin A, increased risk of pseudotumor cerebri with tetracyclines.

Cost : Isotretinoin Cream 0.05 % (20 g) Rs. 38.00-45.00
 Capsules Not freely available
Etretnate Capsules Not freely available

Cyclosporine (see section 8.2.3, Immunosuppressants)

I: Severe forms of psoriasis, allograft rejection, lichen planus, pemphigus, pemphigoid, collagen vascular disorders, Behcet's disease, pyoderma gangrenosum, mycosis fungoides, sezary syndrome.

C/I: Hyper sensitivity.

P/C : Renal impairment, hyper tension, hyperkalemia, acidois, monitoring of serum cyclosporine level.

S/E: Nephrotoxicity, malignancy, hypertension, hepatotoxicity, gastric intolerance and bleeding, hypertrichosis, hyperkalemia.

14.5 ECZEMAS

14.5.1 Topical therapy

Wet compresses-(Saline or Potassium permanganate)

Besides being an astringent potassium permanganate also has disinfectant and deodorising properties. It is bactericidal in vitro.

I: Eczematous condition, acute dermatoses, bromhidrosis, athlete's foot, poisoning dermatitis.

P/C: Do not use for extensive areas (more than 2/3rd of body surface area), concentrated solutions are caustic, not to be used internally and in case of poisoning it has to be carefully treated since death may occur even 1 month from the time of poisoning. Avoid contact with eyes and mucous membranes.

S/E: Maceration, chilling, pneumonitis, irritation and corrosive burns on repeated use

P/A: Powder for topical solution

Dose: 0.01 % solution in wet dressings, 0.02 % solution in water employed as stomach washout in treatment of poisoning by morphine, opium and strychnine.

Cost: Powder (5g) Rs. 4.00 - 5.00

Antibacterial agents (see chapter 2)

Steroids/Corticosteroids (see section 7.5)

14.5.2 Systemic therapy

Antihistamines (see section 6.1.1.1 and 6.1.2.3)

I: Urticarias, Mastocytosis pruritus, preventive dermatitis, atopic dermatitis, eczema, flushing reactions.

Systemic corticosteroids (see section 6.3.1.3)

14.6 PEMPHIGUS

Systemic corticosteroids (see section 6.3.1.3)

Immunomodulant drugs

Dapsone (see section 2.2.11)

I: Hansen's disease, dermatitis herpetiformis, pemphigus, pemphigoid, bullous SLE, vasculitis disorder, acne, rosacea, actinomycosis, malaria, leishmaniasis, PCP in AIDS, pustular psoriasis.

C/I: Hypersensitivity

P/C: Anaemia, leukopenia, G6PD deficiency, pregnancy, lactation

S/E: Haemolytic anaemia, methaemoglobinemia, leukopenia, skin rashes,

fixed drug eruption, Stevens Johnson's syndrome, Dapsone syndrome, phototoxicity, peripheral neuropathy, psychosis.

Immunosuppressive therapy

Methotrexate (see section 8.2.3, Immunosuppressants)

Cyclophosphamide (see section 8.2.3, Immunosuppressants)

Azathioprine (see section 8.2.3, Immunosuppressants)

Chrysotherapy *

Gold salts (Sodium aurothiomalate (see section 8.2.3), Aurothio glucose)

14.7 TOXIC EPIDERMAL NECROLYSIS

Systemic corticosteroids (see section 6.3.1.3)

Wet compresses

14.8 DERMATITIS HERPETIFORMIS

Dapsone (see section 2.2.11)

Sulfapyridine

Colchicine (see section 8.2.4)

14.9 ERYTHEMA MULTIFORME, STEVEN-JOHNSON'S SYNDROME

Topical therapy

Antibacterials (see chapter 2)

Corticosteroid

Systemic therapy

Corticosteroid

Acyclovir - for recurrent EM (see section 2.4.1)

14.10 URTICARIA, ANGIOEDEMA

Antihistamines - H₁ and H₂ receptor blockers. (see section 3.2.1)

Ketotifen (see section 6.3.1.5)

Systemic steroids

Topical antipruritus lotions - eg. Calamine lotion

Danazol (see section 9.7.1.2)

Epsilon amino caproic acid (see section 9.11)

Tranexamic acid (see section 9.11)

Prepared C₁ inhibitor concentrate

14.11 FIXED DRUG ERUPTION

Topical corticosteroids

Antihistamines (see section 6.1.1.1 and 6.1.2.3)

14.12 LICHEN PLANUS

Topical steroids

Dapsone (see section 2.2.11)

Retinoids

Antihistamines (see section 6.1.1.1 and 6.1.2.3)
Griseofulvin (see section 2.3.1, I B)
Metronidazole (see section 14.1.2)
Psoralens with UVA therapy

14.13 PITYRIASIS ROSEA

Topical / systemic corticosteroids
Antihistamines (see section 6.1.1.1 and 6.1.2.3)

14.14 ACNE VULGARIS

14.14.1 Topical therapy

Benzoyl peroxide

I: Acne, rosacea
C/I: Hypersensitivity, ulcerated lesions
P/C: Avoid contact with eyes and mucous membrane. Use with caution in thyroid trouble, eczema and sun burn. Avoid exposure to sunlight.
S/E: Dryness, peeling, blistering, skin irritation, swelling.
P/A: Gel 2.5 %, 5 % w/w
Cream 10 %w/w along with precipitated sulphur 5 %
Dose: For local application 1-2 times daily.
D/I: None reported
Cost: Gel 5 % w/w (20 g) Rs. 25.00 - 30.00
Cream 10 %w/w (20 g) Rs. 29.00 - 30.00
(along with precipitated sulphur 5 %)

Topical antibiotics

Erythromycin (see section 2.2.5)
Clindamycin (see section 2.2.8)
Tetracycline (see section 2.2.4)

Exfoliants

Sulphur

Resorcinol

Anti acne lotion (Precipitated sulphur 3%, salicylic acid 3%, resorcinol 2%, lobocalamine upto 100mL)

Tretinoin (Trans-retinoic acid)

I: Acne, Darier's disease, hidradenitis suppurativa, other keratitic lesion due to disorder of keratinization.
C/I: Acute dermatitis, rosacea, cuts, abrasions
P/C: Avoid contact with mucous membrane, exposure to sunlight,

pregnancy, concomitant use of cosmetics.

S/E: Redness, tightening, itching, exacerbation of signs of infection

14.14.2 Systemic therapy

Antibiotics (see chapter 2)

Tetracycline (see section 2.2.4)

Erythromycin (see section 2.2.5)

Minocycline (see section 14.1.2)

Doxycycline (see section 2.2.4)

Clindamycin (see section 2.2.8)

Estrogens (see section 7.6.1.1)

Ethinyl estradiol (see section 7.6.1.1)

Systemic corticosteroids

Spironolactone (see section 5.7.2.3)

Retinoids

Isotretinoin

Etretinate

Vitamin A (see section 4.2.1)

14.15 HYPOPIGMENTATION

PUVA therapy

L-Phenylalanine - oral solution

Topical khellin.

Cosmetic camouflage - Dihydroxy acetone

Topical and intralesional corticosteroids.

14.16 HYPERPIGMENTATION

Hydroquinone - topical (2 - 5%)

Mono benzyl ether of hydroquinone.

Tretinoin (0.05 - 1%)

Azelaic acid (20%)

14.17 ALOPECIA

Topical / systemic corticosteroids

Dinitrochlorobenzene (DNCB) (contact sensitization)

Dithranol (contact sensitization)

Minoxidil (Topical solution 2 %) (see section 5.7.1)

PUVA therapy

Inosiplex (immunomodulant)

Cyclosporine

14.18 PEDICULOSIS

Permethrin

I: Pediculosis, scabies.

C/I: Hypersensitivity, lactation, infants less than 2 months.

P/C: Avoid contact with eyes, use with caution in pruritus, oedema, erythema.

S/E: Mild transient burning, stinging, pruritus, tingling, rash, erythema.

P/A: Lotion 1%

Cream 5%

Dose: Approximately 30 g to be applied and massaged to the scalp and washed after 10 min (lotion 1 %)

D/I: None reported

Cost: Lotion 1% (60 g) Rs. 29.00 - 55.00

Cream 5% (30 g) Rs. 40.00 - 45.00

Benzyl benzoate

I: Pediculosis, scabies.

C/I: Broken skin, neonates, lactation, pregnancy.

P/C: Clothing and bedding should be changed to prevent reinfection. In children the application should be diluted to minimize the risk of irritation.

S/E: Irritation, allergic dermatitis, drying effect in elderly, CNS convulsions or excitation, urinary retention.

P/A: Emulsions 25 % w/v (50 mL, 100 mL)

Ointment 25 % w/w (25 g)

Dose: Apply to scalp and hair and wash after 24 h. Can be repeated after 1 week, if required.

D/I: None reported.

Cost: Emulsions 25 % w/v (100 mL) Rs. 19.00 - 20.00

Ointment 25 % w/w (25 g) Rs. 10.00 - 12.00

Gamma benzene hexachloride (see section 14.19)

Dose: Apply to scalp and hair and wash after 24 hours. Can be repeated after 1 week if required.

14.19 SCABIES

Benzyl benzoate emulsion.

Dose: Apply all over the body chin down followed by second application

after 24 hours. Scrub bath 48 hours after last application.

Gamma benzene hexachloride

- I: Scabies, Pediculosis
- C/I: Premature neonates, broken skin or mucous membrane, history of seizures.
- P/C: Avoid contact with eyes and use with caution in pregnancy.
- S/E: Eczematous eruptions, dizziness, convulsions, headache, vomiting, loss of sleep.
- P/A: Lotion 1% (50 mL, 100 mL, 1000 mL)
Ointment 1% (15 g, 40 g)
Cream 1% (15 g, 20 g, 25 g)
- Dose: Apply all over the body chin downward, take scrub bath after 12 to 24 hours, may be repeated after 1 week.
- D/I: Haemotoxic agents increase the risk of aplastic anaemia and myeloblastic leukaemia with gamma benzene hexachloride.
- Cost: Lotion 1% (100 mL) Rs. 16.00 - 21.00
Ointment 1% (40 g) Rs. 5.00 - 6.00
Cream 1% (25 g) Rs. 9.00 - 10.00

Crotamiton

- I: Pruritis, scabies, pediculosis.
- C/I: Hypersensitivity, inflamed skin, oozing skin surface, pregnancy and acute exudative dermatitis.
- P/C: Avoid use on fresh inflamed weeping lesion. Do not use on extensive skin areas in infants.
Avoid contact with mouth and eyes. Clothing and bedding should be changed and washed thoroughly.
- S/E: Irritation, allergy, pallor and cyanosis after extensive application.
- P/A: Cream 10%
Lotion 10%
- Dose: Same as for benzyl benzoate
- D/I: None reported
- Cost: Cream 10% (20 g) Rs. 16.00 - 20.00
Lotion 10% (20 g) Rs. 40.00 - 45.00

Permethrin

- I: Scabies, pediculosis
- Dose: Apply all over the body from chin downward after a preliminary bath (cream 5%)

Precipitated sulphur

1 Scabies in infants younger than 2 months of age

14.20 MELANOMA

5 - fluorouracil (topical)

Dacarbazine (DTIC)

Melphelan (perfusion therapy)

14.21 ANTIPERSPIRANTS

Formaldehyde (5 - 10 %) (Side effect - sensitization).

Glutaraldehyde (2% for palms and 10% for soles solutro)

Methenamine (5% stick or 10% solution)

Glycopyrrolate (systemic)

Aluminium chloride hexahydrate (20% in alcohol) (Side effects - stinging, burning, pruritus, ittitation, contact dermatitis).

Scopolamine hydrobromide (0.025%)

4.22 MATERIAL FOR WOUND DRESSINGS

Topical anti bacterial preparations.

MLA cream - topical anaesthetic with adhesive dressing.

Newer surgical dressings - Polyurethane dressings

Hydrocolloid dressings

Hydrogel dressings

Foam surgical dressings.

4.23 ASTRINGENTS

Alamine

I: Pruritus, skin irritation

P/C: For external use only, avoid contact with eyes and other mucous membrane. Discontinue use if sensitivity develops or condition worsens.

P/A: Lotion 8 % w/w

Cost: Lotion 8 % w/w (100 g) Rs. 28.00 - 30.00

Aluminium acetate

Used as an astringent in ear infections

Zinc oxide

I: Eczema, excoriation

P/A: Compound zinc paste

Zinc oxide ointment

Zinc cream

Various other preparations are also available.

Cost: Cream 8.5% w/w (15 g) Rs. 20.00 - 25.00

CHAPTER 15 : DRUGS USED IN PAEDIATRIC PRACTICE

15.1 PRESCRIBING FOR CHILDREN

Children and neonates differ from adults in the way they handle and respond to drugs.

It is always important to state the age and if possible weight of the child while writing a prescription for a child. The dosage for children is adjusted from adult dose by using either age/body weight/body surface area. Although Body surface area is a more accurate method of calculating the dose, in practice, dose is generally calculated and expressed in mg/kg of body weight. Because of their higher metabolic rate children need higher dose per kilogram than adults. Children over 12 years generally require the adult dose. This method based on weight can cause problem in obese children as they may get higher dose than required. Under such circumstances it is better to calculate dose based on ideal body weight for that age rather than the actual weight.

Body weight of children: 1 year - 9 kg.

Add 2 kg for every year up to 7 years i.e. at 7 year it is $9 + 12 = 21$ kg . Then add 2.5 kg for every year upto 12 years.

Surface Area from Age in M^2 :

Table showing age and surface area of children

Age	At Birth	3 months	1 year	3 years	6 years	9 years	10 years	Adult
Surface area in m^2	0.15	0.30	0.45	0.60	0.75	0.90	1.00	1.73

Doctors can be under considerable pressure from parents and drug companies to overprescribe. This, however, should be resisted. Rational drug therapy in children requires an understanding of the pharmacokinetics-what the body does to a drug-and the pharmacodynamics-what the drug does to the body. Drug which is safe and well tolerated by the mother may be potentially harmful and damaging to the foetus. Similarly, drug excreted in breast milk, although in small amounts, may adversely affect the suckling infant. Risk of toxicity in neonates and young infants is increased by insufficient renal function, differing organ sensitivity, relative enzyme deficiencies and inadequate detoxifying system leading to delayed excretion of drugs. The total daily dose and frequency of administration in neonates, therefore, needs modification. Monitoring of blood level of drugs, especially for theophylline, aminoglycosides and anti-convulsants is invaluable in the management, wherever possible.

The dose of some commonly used drugs in children are given below. The reader is advised to refer to appropriate section for detailed description or

indications, contraindications, precautions and drug interactions. Where relevant, the important indication of a particular drug is highlighted along with the dosage.

15.1.1 Antibacterials

Ampicillin

P/A: Capsule	250mg, 500mg.
Paediatric tablet dispersible	125mg.
Suspension	125 mg, 250 mg/5 mL
Injection	250mg, 500 mg vials.
Dose: Newborn below 1 week	50 mg/kg/24 h, 8-12 h
More than 1 week	100 mg/kg/24 h, 6 h
Newborn Meningitis	200 mg/kg/24 h, 4 h
Over 2 months- usual dose	50-100 mg/kg/24 h, 6 h oral / i.v. or i.m.
Septicaemia	200 mg/kg/24 h, 6 h, i.v. initially.
Meningitis	300- 400 mg/kg/24 h, 4 h, i.v. initially

Amoxycillin

P/A: Capsule	250 mg.
Kid tablet	125mg
Suspension	125 mg, 250 mg/5 mL
Drops	100 mg/mL.
Dose: 25-50 mg/kg/24 h, 8 h oral	
Parenteral preparation also available.	

AMOXYCILLIN+ CLAVULANIC ACID

P/A: Syrup	125 mg + 31.25 mg (156.25 mg in 5 mL).
Tablet	250 mg + 125 mg (375mg), and 500 mg + 125 mg(625mg).

Dose: 25-50 mg/kg/24 h, 8 h of Amoxycillin, oral/parenteral.
Expensive, but effective orally even in severe infections.

Cephalosporins

All are expensive and has limited use when given orally. Third generation cephalosporins are very effective in serious infections and usually given parenterally

Cephalexin

P/A: Drops	100 mg/mL.
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Syrup 125, 250 mg/5 mL.

Capsule 250, 500 mg

Dose: 25-100 mg/kg/24 h, 6 h oral

Cefazoline

Dose: 50-100 mg/kg/24 h, 6-8 h i.v. or i.m.

Cefadroxil

P/A: Syrup 125, 250 mg/5mL

Tablet 250, 500 mg.

Dose: 30mg/kg/24h, 12 h oral.

Cefaclor

P/A: Drops 100mg/mL

Syrup 125 mg, 187mg/ 5 mL.

Capsule 250 mg.

Dose: 20 - 40 mg/kg/24 h, 8 h oral.

Cefixime

P/A: Capsule 100mg, 200mg

Syrup 50, 100 mg/5 mL.

Dose: 8mg/kg single or in two divided dose.

3rd generation cephalosporins are available for oral use - Expensive but effective in serious infections.

Ceftriaxone

Dose: 50-75 mg/24 h, o.d. i.v./i.m.

Meningitis 100 mg/kg/24 h, 12 h i.v. or i.m.

Generally considered the drug of choice in pyogenic meningitis in children.

Cefotaxime

Dose : 100-200 mg/kg/24 h, 8 h

Meningitis 200 mg/kg/24 h, 6 h i.v. initially

Very safe and effective in severe infections.

Ceftazidime

Dose: 100-150 mg/kg/24 h 8 h i.v. or i.m.

Meningitis- 225 mg/kg/24 h every 8 h i.v. or i.m.

Effective in serious gram negative infections including pseudomonas in immuno compromised patients.

Chloramphenicol

P/A: Capsule 250 mg and 500 mg

Syrup 5 mL = 125 mg

Injection 1 g, 2 g/10 mL.

Dose: Standard - 50 mg/kg/24 h, 6 h, oral or i.v. or i.m.

Meningitis-100 mg/kg/24 h, 6 h.

Useful in typhoid fever and effective drug for meningitis and pneumonia.

Aplastic anaemia is very rare in Indian children.

Cloxacillin

P/A: Capsule 500 mg and 250 mg.

Suspension 125 mg/5 mL.

Injection 250,500mg/vial

Dose: 50-100 mg/kg/24 h, 6 h (upto 200 mg/kg/24 h in severe infection).

Drug of choice in staphylococcal infection.

Erythromycin

P/C: Drug induced gastritis is common; avoid in liver diseases.

P/A: Tablet 250 mg, 100 mg.

Suspension 125mg/ 5mL

Drops 100 mg/mL.

Dose: 40-50 mg/kg/24 h, 6 h.

Gentamicin

P/A: Injection 1 mL = 40 mg and 80 mg.

Dose: Newborn below 1 week-5 mg/kg/24 h, 12 h

Child 5-7.5 mg/kg/24 h, 8 h i.v. or i.m.

Monitor renal function and dose adjustment required in renal failure for all aminoglycosides.

Amikacin

P/A: Injection 100 mg, and 500 mg/2 mL.

Dose: Newborn below 7 days - 15 mg/kg/24 h, 12 h i.m. or i.v.

Above 7 days and children - 15 - 20 mg/kg/24 h, 8-12 h i.m. or i.v.

Netilmycin

P/A: Injection 10, 25, 100 mg/mL.

Dose: 5-7.5 mg/kg/24 h, 8 h i.m.

Kanamycin.

P/A: Injection 500 mg, and 1 g/vial

Dose: 15 mg/kg/24 h, 12 h i.m.

Rarely used now.

Azithromycin

P/A: Syrup 200mg/5mL

Capsule 250mg

Dose: 10mg/kg single dose daily oral for 3 days. Expensive but very convenient for administration in children because of single dosage and short duration of therapy

Penicillin (Pencillin G and Pencillin V)

P/A: Oral and Parenteral

Tablet 125 mg, 250 mg

Dose: Penicillin G

New born below 1 week - 50,000 units/kg/24 h, 12 h.

Above 1 week 100,000 units/kg/24 h 6 h.

Meningitis 300,000 units/kg/24 h 4 h i.v.

Standard dose 50,000 units/kg/24h, 6 h i.v. or i.m.

Severe infections-200,000 units/kg/24h, 6 h

Meningitis beyond neonatal period- 400,000 units/kg/24 h, 4 h

Procaine Penicillin: 25-50,000 units/kg/24 h, i.m. daily.

Benzathine Penicillin. Below 6 years- 6 lakhs units i.m. x 3 weekly

Above 6 years-12 lakhs i.m. x 3 weekly.

Penicillin V.

Tablets 125-250 mg: 125 mg=200,000 units

Dose: 25,000-50,000 units/kg/24 h, 6 h

Rheumatic Prophylaxis 250mg b.d.

Sulfadiazine

P/A: Tablet 500 mg

Dose: 150 mg/kg/24 h, 6 h

Rarely used at present except for Rheumatic Prophylaxis - 500 mg b.d.

Co-trimoxazole (trimethoprim, sulphamethoxazole 1:5 ratio)

P/A: Tablets Trimethoprim(TMP) 80 mg and 160 mg

Paediatric tablet 20 mg.

Suspension 40 mg TMP/5 mL

Injection 5 mL =80 mg

Dose: Oral 6-8 mg/kg/24 h, 12 h 10 days.

i.v. 6mg/kg/12 h as infusion.

15. Drugs Used in Paediatric Practice

Severe infections and pneumocystitis pneumonia. 15 - 20 mg/kg/24 h (based on trimethoprim) 6-8 h for 14 days.

Furazolidone

S/E: Drug induced gastritis common with high dose

P/A: Tablet 100 mg
Suspension 35 mg/5 mL.

Dose: 6 mg/kg/24 h 6-8 h.

Typhoid : 15 mg/kg/24 h, 6 h.

Ciprofloxacin

P/A: Tablet 250 and 500 mg

Used in multidrug resistant typhoid and cystic fibrosis. Not recommended in children due to possible risk of injury to growing cartilage

Dose: 20-30 mg/kg/24 h given as 2 doses 12 h oral or i.v. infusion

Nalidixic Acid

P/A: Tablet 500 mg

Syrup 300 mg/5mL

Dose: 55 mg/kg/24 h 6-8 h

15.1.2 Anthelmintics

Albendazole has broad spectrum of activity, safe and single dose is effective against most intestinal worms. It is the preferred drug for children due to convenience of use and safety. For children living in unhygienic environment, deworming may be done every 6 months. Mebendazole and albendazole may cause worm migration and lead to vomiting of round worms. Therefore it is better to use pyrantel or piperazine initially when mixed worm infestation is suspected. Pyrantel pamoate and piperazine are mutually antagonistic in their action on round worms and therefore they should not be prescribed simultaneously. Both drugs are hepatotoxic as well and they should be avoided in the presence of existing liver disease.

Albendazole

P/A: Tablet 400mg
Suspension 200mg/5 mL.

Dose: Below 2 years- 200 mg single dose.

Above 2 years- 400 mg single dose

For strongyloidiasis / H. nana / Taeniasis- 400 mg daily x 3 days.

Levamisole

P/A: Tablet 50mg, and 150 mg.

Syrup 50 mg/mL.

Dose: For ascariasis-2.5 mg/kg/single dose.

For hookworm - 3.5 mg/kg/6 h x 4 doses.

Piperazine

P/A: Tablet 500 mg.

Syrup 5mL =750 mg.

Dose: Round worms-75 mg/kg/dose 2 consecutive days.

Pinworm -50 mg/kg/dose x 7 days

Pyrantel Pamoate

P/A: Syrup 5 mL = 250 mg/150 mg.

Tablet 200mg/250 mg.

Dose: Broad spectrum antihelminthic - 11 mg/kg/dose x single dose.

Can be repeated after 2 weeks in enterobiasis.

Mebendazole

P/A: Tablet 100mg.

Syrup 100 mg/5 mL.

For use only in children above 2 years.

Dose: 1 tab.(100 mg)b.d. for 3 days irrespective of age.

Diethylcarbamazine

P/A: Plain tablet 50 mg, forte = 100 mg.

Syrup 120 mg/5mL.

Paediatric syrup 50mg/5mL.

Dose: 10mg/kg/24 h, x t.d.s x 14 days for Tropical eosinophilia.

6 mg/kg/24 h, 3 divided dose daily x 21 days for Filariasis.

15.1.3 Antiprotozoal agents

Metronidazole

P/A: Tablet 200 mg, and 400 mg.

Suspension 100/200 mg = 5mL.

Injection 5 mg = 1 mL.

Dose: Amoebiasis- 30 mg/kg/24 h, 8 h, 10 days (Tissue amoebicide).

Giardiasis - 25 mg/kg/24 h, 8 h, 5 days.

Parenteral-7.5 mg/kg/dose 8 h.(anaerobic infections)

Tinidazole

P/A: Tablet 300 mg, and 500 mg.

Dose: 20-30 mg/kg/24 h in 2 divided doses, 5-10 days

Diloxanide furoate

P/A: Tablet 500 mg.

Dose: 20 mg/kg/24 h x 8 h, 10 days (in asymptomatic cyst passers)

Chloroquine

P/A: Tablet 150 mg base.

Dose: Day 1-10 mg/kg/initially; 5 mg/kg after 6 hrs.

Days 2 and 3, 5 mg/kg o.d. (uncomplicated malaria).

Prophylaxis - 5 mg/kg once a week.

Quinine Sulphate

P/A: Tablet 300mg

Injection 300mg/mL.

Dose: Cerebral malaria: 20mg/kg i.v. diluted initially over 4 h followed by 10mg/kg every 8 h i.v. slowly over 2-4 h until oral intake is possible. Oral dose 8mg/kg every 8 h for 7 days.

Primaquine

P/A: Tablet 2.5 & 7.5mg

Dose: 0.25mg/kg daily for 2 weeks following treatment with chloroquin.

This is to prevent relapse in Vivax malaria.

Pyrimethamine

P/A: Tablet 25mg + sulfadoxime 500mg combination.

Dose: In resistant malaria dose upto 4 yrs -1/2 tablet.

Older children upto 9 yrs 1 tablet; >9yrs 2 tab all in single dose.

15.1.4 Antituberculosis drugs

Isoniazid (INH)

P/A: Tablet 100 mg, and 300 mg;

Liquid 100 mg/ 5 mL.

Dose: 5-10 mg/kg/day, single dose.

Rifampicin

P/A: Capsule 150 mg, and 300 mg.

Suspension 100 mg/5 mL.

Dose: 10-12 mg/kg/24 h, single dose 30 min before breakfast/along with INH

Ethambutol

P/C: Watch for visual failure.

P/A: Tablet 200 mg, and 800 mg.

Dose: 20 mg/kg/day, single dose
Not recommended below 3 years.

Pyrazinamide.

Dose: 25-35 mg/kg/24 h, b.d. or t.d.s. oral.

Para Amino Salicylic acid (PAS)

P/A: Tablet 1 g.

Granules 1 spoon = 2 g.

Dose: 200-300 mg/kg/day in divided doses.

Very seldom used.

Streptomycin

Dose: 20-40 mg/kg/day i.m.

Rarely used.

15.1.5 Antipyretic analgesics

Paracetamol

P/A: Tablet 500 mg.

Syrup 25 mg, 250 mg/5 mL.

Injection 150 mg/1 mL.

Dose: 40 mg/kg/24 h, 4-6 h; 5 mg/kg/single dose i.m..

Aspirin

P/A: Tablet 75 mg, 300 mg

Dose: Anti-pyretic - 40-60 mg/kg/24 h, 4-6 h.

Not recommended in very young children due to risk of Reye's syndrome.

Anti-rheumatic - 100 mg/kg/24 h, 6 h after food.

Ibuprofen

P/A: Tablet 200 mg, and 400 mg.

Suspension 100mg/5 mL.

Dose: 20-40 mg/kg/24 h, 8 h.

Mefenamic acid

P/A: Capsule 250 mg, and 500 mg.

Syrup 50 mg/5 mL.

Dose: 25 mg/kg/24 h, 8 h.

Safety and efficacy in children is not established.

Nimesulide

P/A: Tablet 100 mg;

Suspension 50 mg/5 mL.

Dose: 5 mg/kg/24h divide into 2-3 doses.

Avoid if liver dysfunction is suspected.

15.1.6 Antispasmodics

Atropine

P/A: Injection 0.6 mg/mL.

Dose: 10-20 mcg/kg/dose i.m. or i.v.

Dicyclomine Hydrochloride

P/A: Tablet 20mg,

Syrup 10 mg/5 mL.

Drops 10 mg/mL.

Dose: Infants- 5 drops/dose; older children - 0.5 mg/kg/dose.

Infantile colic rarely needs treatment.

Not suitable for use in younger children.

Cisapride

P/A: Tablet 10mg;

Syrup 5mg/5mL.

Dose: 0.2mg/kg x q.d.s. 15 min before feed.

Cisapride is a prokinetic agent and is not an antispasmodic. It facilitates gastric motility and increases lower oesophageal sphincter tone. Effective in gastro-oesophageal reflux and recurrent functional abdominal pain in children.

Hyoscine Butylbromide

P/A: Tablet 10mg;

Injection 20mg/mL.

Dose: >6years 1 tab x t.d.s. or 0.5 mL i.m. or i.v.

15.1.7 Antihistaminics/antiemetics

Anti-emetics are seldom used in children. Extrapyrimal side effects easily occur when the recommended dose is exceeded manifesting as dystonia and oculogyric crisis. This can be controlled with phenergan or diazepam.

Promethazine.

P/A: Syrup 5mg/5 mL.

Injection 25mg/mL.

Dose: 0.5 mg/kg/dose.

Metoclopramide

P/A: Tablet 10mg.
Injection, 5 mg/mL
Syrup 5 mg/5 mL.

Dose: 0.1-0.2 mg/kg/dose i.m./oral.

Domperidone.

P/A: Tablet 10 mg.
Suspension 1 mg/mL.

Dose: 0.2 - 0.4 mg/kg/dose, may be repeated.

Less chance for extra pyramidal side effects.

Cyprohepatidine

P/A: Tablet 4mg
Syrup 2 mg/5 mL.

Dose: 0.25 mg/kg/24 h, 8 h oral.

Common side effect is drowsiness. Used as an appetite stimulant and is effective in prevention of migrainous headache.

Pheniramine Maleate

P/A: Tablet 25, 50mg;
Syrup 15 mg/5mL
Injection 22.75mg/mL.

Dose: 1 mg/kg/24 h, 8-12 h oral or i.m. or i.v.

May cause drowsiness.

Diphenhydramine

P/A: Tablet 25, 50mg.
Syrup 12.5 mg/5 mL.
Dose: 5 mg/kg/24 h, 8 h oral.

Astemizole

P/A: Tablet 10 mg.
Syrup 5 mg/5 mL.
Dose : 0.2-1.0 mg/kg/day single dose.

Cetirizine

P/A: Tablet 10mg
Syrup 5 mg/5mL.
Dose: 2 - 6 years 5mg daily; above 6 years 10mg daily.
Less drowsiness compared to other antihistamines.

Loratidine

P/A: Tablet 10mg
Syrup 5 mg/5mL.

Dose: >30kg -10 mg;<30 kg -5 mg o.d.
Considered to be non-drowsy.

15.1.8 Bronchodilators

Aminophylline

P/A: Injection 250 mg/10 mL.

Dose: 6 mg/kg/dose initially i.v. diluted with equal volume of fluid every 6 h or follow on with 0.7-0.9 mg/kg/h as continuous infusion. If child already had theophylline in preceding 4 h, then reduce initial bolus dose to 3 mg/kg. Therapeutic plasma concentration 10-20 mg/L; it has narrow margin of safety.

Hydroxy Ethyl Theophylline (Deriphylline)

P/A: Tablet 100 mg
Syrup 60 mg/5 mL
Injection 220 mg/2 mL.

Dose: 12 mg/kg/24 h divided 8 h; oral or i.m.

Adrenaline

Dose: 0.01 mL/kg of 1:1000 solution, s.c.; can be repeated after 20 min.

Note: Terbutaline has similar action and less side effects and is the preferred drug in asthma.

Salbutamol

P/A: Tablet 2 mg, 4 mg
Syrup 2 mg/5mL

Slow release capsules: 4, 8mg.

Inhaler 100 mcg/metered dose. 200 mcg/rotacap (dry powder inhaler).

Respirator solution: 5 mg/mL.

Dose: 0.2 mg/kg/24 h x 8 h oral; 1-2 puff of 100 mcg MDI every 4-6 h or 1 rotacap (200 mcg) every 4-6 h. Nebulize respirator solution 0.1-0.2 mg/kg diluted with N saline or in older children 0.5 mL respirator solution diluted with 4 mL N saline every 4 h or earlier.

Terbutaline

P/A: Tablet 2.5 mg, 5 mg;

Syrup 1.5 mg/5 mL.

Respirator solution 10 mg/mL.

Injection 500 mcg/mL.

Inhaler 250 mcg/metered dose.

Dose: 0.1-0.15 mg/kg/24 h, 8 h oral; 5 mcg/kg/dose s.c.

Repeat in 20 min if needed. Terbutaline inhaler 1-2 puffs of 250 mcg every 4-6 h. In severe cases not responding to nebulization, continuous i.v. infusion diluted with 5% dextrose can be used. i.v. dosage 10 mcg/kg bolus diluted, followed by 0.4-0.6 mcg/kg/min increasing slowly every 15 min by 0.2 mcg/kg/min to a maximum of 3-6 mcg/kg/min.

Ipratropium Bromide

P/A: Metered dose inhaler 20 mcg/puff;

Respirator solution 250 mcg/mL.

Dose: 1-2 inhalations every 4-6 h or in acute severe asthma respirator solution 0.5-1mL nebulized every 4-6 h.

15.1.9 Prophylaxis of asthma

Ketotifen

P/A: Tablet 1 mg.

Syrup 1 mg/5 mL.

Dose: 1 to 2 years - 2.5 mL b.d.

More than 2 years - 1 mg, b.d. Useful in mild episodic asthma accompanied by recurrent URI.

Sodium Cromoglycate

P/A: Capsule 20 mg.

Dose: Metered dose inhaler 1 mg/puff, 1 capsule 6-8 h or 1-2 puff metered dose 6-8 h.

Budesonide

P/A: Metered dose 100, 200 mcg/puff

Rotacap 100, 200 mcg

Dose: 100 to 200 mcg b.d. for about 6 months or until control is achieved and then slowly step down.

Used in children with a spacer or an improvised device like a plastic coffee cup. Very effective with negligible systemic side effects.

Beclomethasone Dipropionate

P/A: Metered dose inhaler 50,100, 200 mcg/actuation.

Dose: 50 to 200 mcg t.d.s - q.d.s. depending on severity of symptoms and response.

Sustained Release Theophyllin

P/A: Tablets/spansules 100, 125, 150, 200, 300mg.

Dose: 15-20 mg/kg/24h in 2 divided dose.

15.1.10 Anticonvulsants

Phenobarbitone

P/A: Tablet 30 mg, 60 mg, 100mg

Injection 200 mg/mL.

Dose: To control convulsions-Loading dose 15-20 mg/kg/i.m or i.v.

Usual dose-3-8 mg/kg/24 h, 12 h or once daily.

Diazepam

P/A: Tablet 2mg, 5 mg, and 10 mg.

Syrup 2mg/5 mL.

Injection 5 mg/mL.

Dose: 0.2-0.5 mg/kg/dose i.v./oral.

Rectal dose 0.25 -0.5 mg/kg using a feeding tube and syringe.

Continuous infusion in status - 50mg in 500 mL 5% dextrose 0.1mg/kg/h.

Dilantin Sodium

P/A: Capsule / tablet 100mg.

Syrup 125 mg/5 mL.

Injection 100 mg/mL.

Dose: To control convulsions, loading dose - 15-20mg/kg/i.v.

Usual dose - 5-8 mg/kg/24 h 12 h/single dose.

Paraldehyde

Dose: 0.15 mL/kg deep i.m. Not available at present, but if available still an excellent drug in status epilepticus.

Carbamazepine

P/A: Tablet 100 mg, 200 mg, and 400 mg.

Syrup 100 mg/5mL.

Dose: 10 - 20 mg/kg/24 h, 8-12 h.

Sodium Valproate

P/A: Tablet 200 mg, 500 mg.

Syrup 200 mg/5 mL.

Dose: 15-40 mg/kg/24 h, 6-12 h divided dose.

Rectal: 20mg/kg 1:1 dilution with tap water as retention enema.

Lorazepam

Useful in status epilepticus;

Dose: Loading dose 0.1 mg/kg i.v. rate of infusion 1-2 mg/h in normal saline or 5% dextrose.

Midazolam

Less cardio - respiratory arrest than with diazepam.

Dose: 0.05-0.2 mg/kg as loading dose i.v./i.m.

Infusion 0.1 to 0.4 mg/kg/h in N. saline or 5% dextrose is effective in status epilepsy.

15.1.11 Sedatives

Diazepam

P/A: Injection 5mg/mL i.m.

Oral 2mg/5 mL

Dose : 0.25 - 0.5/kg single dose.

Promethazine Hcl

P/A: Injection 25 mg/mL i.m..

Syrup 5 mg/5 mL.

Dose: Single dose-0.5 mg/ kg.

Morphine

P/A: 10 mg, 15 mg, and 30 mg/mL.

Dose: 0.1-0.2 mg/kg/dose i.m or s.c..

Pethidine

P/A: 50 mg/mL.

Dose: 2 mg/kg/dose. i.m. or i.v.

Pentazocine

P/A: Tablet 20 mg.

Injection 30 mg/mL.

Dose: Up to 0.5 - 1.0 mg/kg/dose i.m. or s.c.

Not recommended for children less than 12 years.

Trimeprazine tartarate

P/A: 30 mg/5 mL.

Dose: Single dose-2-4 mg/kg.

Triclofos (pedicloryl)

P/A: 500mg/5mL.

Dose: <1year 100 to 250 mg/dose.

>1year 250 to 500 mg./dose.

15.1.12 Cardiovascular drugs / antihypertensives

Digoxin

P/A: Tablet 0.25 mg.

Syrup 1 mL = 0.05 mg (1/5th of tab.).

Dose: (digitalising) New born - 0.03-0.05 mg/kg; 1 month - 2 years - 0.04-0.06 mg/kg.

Above 2 years - 0.04 mg/kg, half the dose initially, $\frac{1}{4}$ dose at 8 h, $\frac{1}{4}$ at 16 h.

Maintenance dose: $\frac{1}{4}$ - $\frac{1}{5}$ th of digitalising dose given as single or twice daily dose to be started 12 h after the last digitalising dose.

i.v. digitalising dose: 75% of oral dose. i.m. route not preferred.

Frusemide

P/A: Tablet 40mg.

Injection 2 mL = 20 mg.

Dose: 1 mg/kg (parenteral) upto maximum 2 mg/kg/24h.

Oral dose 1-3 mg/kg/day.

Hydrochlorothiazide

Dose: 2-3 mg/kg/day.

Spirolactone.

Dose: 2-3 mg/kg/day: single dose or 8 h.

Nifedipine.

P/A: Capsule 5mg, and 10 mg and tab. 10 mg.

Dose: 0.5-1.0 mg/kg/day x 8 h : emergency 0.5 mg/kg/dose sublingual.

Propranolol

P/A: Tablet 10mg, 40mg and 80mg tab.

Dose: 1-4mg/kg.

Main indications in children are to prevent cyanotic spell in children with Tetralogy of Fallot and to reduce portal venous pressure in infrahepatic portal hypertension.

Atenolol.

P/A: Tablet 25mg, 50mg, 100mg.

Dose: 1 mg/kg initially raising to 2 mg/kg if required o.d.

Safety not established for children.

Captopril.

P/A: Tablet 25 mg.

Dose :0.5 to 2mg/kg t.d.s. before meals.

Enalapril.

P/A: Tablet 2.5mg, 5mg, 10mg, 20mg.

Dose : 0.1- 0.5mg/kg/24h o.d. or b.d.

Dopamine.

1 ampoule = 200 mg(200,000 mcg). 1 mL : 40 mg, action is dose related.

Dose: To improve renal perfusion-2-5 mcg/kg/min infusion; for pressure effect 5-10 mcg/kg/min. Begin with 5 mcg/kg/min and build up to 20 mcg/kg/min. Solution used should be saline or dextrose. Do not add soda bicarb to the infusion. Dose $6 \times \text{wt in kg} = \text{mg dopamine}$. This amount added in 100 mL 5% dextrose. 1mL/h will deliver 1 mcg/kg/min.

CHAPTER 16 : GYNAECOLOGY

16.1 NUTRITIONAL REQUIREMENT IN PREGNANCY

Diet in pregnancy should be light, digestible, nutritious and rich in proteins, vitamins and minerals.

The dietary requirements in pregnancy

Total calories - 2200 - 2500 Kcals.

Proteins- 55 g, Fat 40 g

Half of the protein should be first class protein containing essential aminoacids. Fat should include animal fat which contains Vitamins A & D. Daily diet should generally include 1/2 litre of milk, one egg, green leafy vegetables and fruits. Along with this supplementation of minerals and vitamins must be given.

16.1.1 Ideal diet prescribed for antenatal woman

National Institute of Nutrition (ICMR)

Diet for pregnant women

Food stuff	Light Work	Moderate work
Cereals	445 g	475 g
Pulses	55 g	60 g
Green leafy vegetables	100 g	100 g
Other vegetables	40 g	40 g
Roots and tubes	50 g	50 g
Milk	200 mL	250 mL
Fat and oil	20 g	20 g
Sugar and jaggery	30 g	30 g
Calories	2200 K. cal	2500 K. cal
Protein	70 g	75 g
Fat	40 g	50 g

Non vegetarians substitute pulses with 2 egg / 50 g fish or meat plus 10 g fat.

The pregnant women should be advised to have her usual diet with additional provisions of green leafy vegetables, fruits, milk, and eggs. It is better to have snacks in between principal meals.

16.2 DRUGS AND PREGNANCY

Drugs should be used in pregnancy with caution. Certain drugs are absolutely contraindicated in pregnancy.

16.2.1 Drugs to be avoided in 1st trimester

Thalidomide, androgen and androgen derivatives, diethyl stilbesterol, tetracyclines, warfarin, folate antagonists like methotrexate.

16.2.2 Drugs which are possibly teratogenic and better avoided in pregnancy unless absolutely indicated

High dose aspirin, quinine derivatives, fluoroquinolones, indomethacin, lithium, phenytoin, gaseous general anaesthetics.

16.2.3 Drugs to be avoided in 3rd trimester as far as possible

Aminoglycosides, tetracyclines, beta blockers.

Aminoglycosides and betablockers may be used with caution where it is absolutely indicated.

16.2.4 Drugs contraindicated in lactation

Indomethacin, norfloxacin, lithium, antimalignancy drugs.

16.3 DOS AND DON'T IN PREGNANCY

16.3.1 Confirmation of pregnancy can be done by

1. Urine test :
 - a. card test - as early as 3 - 5 day after missed period
 - b. pregcolor
 - c. gravindex test
2. Vaginal examination - as early as 6 weeks of pregnancy
3. Ultrasound examinations - from 5 weeks onwards.

16.3.2 Pattern of antenatal visits

First visit in the first trimester as early as 1 - 2 weeks after missing menstrual period. This is for confirmation of uterine pregnancy and for excluding other pathology like ectopic gestation, tumors, complicating pregnancy etc. Then the pregnant woman should be examined once in every months until 28 weeks, once in 2 weeks till 36 weeks and thereafter once in a week.

16.3.3 What should be done at each visit

Detailed history about present and past pregnancies, past medical and surgical illness, diseases and congenital anomalies in the family should be taken. Socioeconomic status of the patient should be assessed.

A general and systemic examination should be done and then a detailed obstetric examination. In the later weeks of pregnancy, obstetric examination

should be made to assess the lie, presentation and position of the foetus. A vaginal examination should be done for a primigravidae near term to assess cephalopelvic disproportion.

16.3.4 Basic investigations to be done

This includes Hb estimation, Blood group and Rh, VDRL and urine for albumin and sugar. A glucose challenge test should be done for all pregnant women in the late 2nd trimester, to detect impaired glucose tolerance and gestational diabetes mellitus (GDM).

Glucose challenge test (GCT) is done by estimating random blood sugar 1 h after 50 g of oral glucose. If value is 130 or above a glucose tolerance test (GTT) should be done.

A routine ultra sound scanning examination is advisable for all pregnant women by around 18 - 20 weeks of gestation. This will help to assess gestational age correctly and also to rule out gross congenital anomalies. But ultra sound examination (USE) is not a substitute for clinical assesment.

X-ray should not be taken in pregnancy unless absolutely indicated.

16.4 OXYTOCICS

Oxytocics are drugs which make the uterus contract. They are used for induction of labour and abortions and also to treat post partum haemorrhage.

Oxytocin

- I: Induction of labour, uterine inertia, postpartum haemorrhage, abortion.
- C/I: Cephalopelvic disproportion. In grand multipara, previous cesarian section should be used with great caution.
- P/C: Monitor maternal and foetal cardiovascular status. Also see the uterine tone, adjust the rate of infusion accordingly.
- S/E: Hypertonic uterine contraction and rupture of uterus can occur if given without adequate supervision foetal hypoxia.
- P/A: Injection 5 iu
- Dose: 5 units diluted in 500 mL of 5% glucose or saline i.v. infusion
- D/I: Pressor effect of sympathomimetics may be increased by oxytocin leading to postpartum hypertension. With prostaglandins there is risk of uterine rupture and cervical lacerations. With ergotamine synergistic effect in control of postpartum haemorrhage.
- Cost: Inj 5 iu (1mL) Rs. 4.00- 11.00

This is used for induction and acceleration of labour, in inevitable abortion and also for treating atonic PPH. This is usually given as i.v. infusion.

Methyl Ergometrine

- I: To hasten placental separation, to reduce III stage haemorrhage, to treat atonic PPH.
- C/I: Coronary and peripheral vascular disease, pregnancy, cardiovascular disease.
- P/C: Avoid in hepatic and renal insufficiency.
- S/E: Thrombosis, gangrene
- P/A: Tablets 0.125 mg
Injection 0.2mg, 0.5mg/mL
- Dose: Oral 0.25 mg
i.v. 0.2 - 0.5mg
- D/I: Risk of vascular occlusion increased with beta blockers, methysergide, and smoking.
Erythromycin increases the plasma concentration of ergot alkaloids.
Oral contraceptives increases the risk of thrombosis.
- Cost: Tab 0.125 mg (10) Rs.18.00- 37.00
Inj 0.2mg (1mL) Rs. 5.00- 7.00
- Methyl ergometrine is used intravenously in the 2nd stage of labour in cephalic presentation as the anterior shoulder of the baby is being delivered. This is for reducing 3rd stage haemorrhage and also to hasten placental separation. It is also used as a first line of treatment for atonic PPH, where it is given as i.v. or i.m. bolus dose.

Prostaglandin

- PGF 2 alpha is the drug that is used. Given as i.m. injection for treatment of PPH.
- I: Therapeutic abortion, in postpartum bleeding, induction of labour.
- C/I: Cardiac, hepatic, pulmonary and renal diseases.
- P/C: Raised intraocular pressure, hypertension, diabetes, epilepsy.
- S/E: Nausea, vomiting, diarrhoea, fever.
- P/A: Injection 0.5 mg,
Tablet 0.5 mg
- Dose: 0.25mcg/min i.v. given in normal saline
- D/I: Enhanced efficacy of oxytocics leading to uterine rupture.
Antiprogestins enhance the efficacy.
- Cost: Inj 0.5 mg 1 disposable syringe Rs.170.00
Tab 0.5 mg 4 Rs. 139.00
- PGF 2 gel is used for cervical ripening as local application to cervical canal

16.4.1 Induction of Labour

Labour is induced for various indications :

The common indications are

1. Post dated pregnancy
2. Pregnancy induced hypertension and pre eclampsia.
3. Intra uterine growth restriction and foetal compromise - when the continuation of intra uterine life is unfavorable for the foetus.
4. Intra uterine demise of the foetus.

Methods of Induction can be medical and surgical

Medical methods - several drugs are used

Oxytocin

It is given as an i.v. infusion with 2.5-5 iu in 500 mL of 5% dextrose saline or normal saline.

The drip is started with a rate of 4 drops per minute and slowly increased until effective contractions are established.

Advantages are:

1. The dose of the drug can be adjusted.
2. Cheap and easily available.
3. Side effects are minimal.

How to monitor the patient who is on oxytocin drip

1. Watch uterine contractions - duration, intensity and interval.
2. Ensure that uterus relaxes in between contractions. If uterus remains tonically contracted, the infusion should be stopped.
3. Foetal heart rate, maternal pulse and temperature should be noted.

Infusion should be stopped

1. If there is hypertonic uterine contractions.
2. Bradycardia or irregularity of foetal heart rate.
3. Maternal tachycardia or fever.

Note: When labour is induced or augmented with oxytocin, the drip should be continued after delivery. The dose should be increased to 10 units/ 500 mL to prevent PPH.

Prostaglandins

- a. PGE₂(Primiprost) 500 mg tablets are available. One tablet is given by mouth every hour until good contractions are established or upto a maximum dose of 4 tablets. Advantage is that there is no need for i.v. drip and its complications like pyrexia, thrombophlebitis etc. Disadvantage is that, there is no control over the dose since it is orally administered.
- b. PGE₂ gel (0.5mg)

This is administered intra cervically. It is relatively convenient and effective

method of induction of labour. But this drug should not be used if there is a history of bronchial asthma.

Surgical method of induction

This is by a low rupture of membranes.

Conditions to be satisfied

Cervix should be partially effaced and at least 1 cm dilated. Presenting part must be vertex and fixed at the brim of the pelvis.

16.4.2 Induction of abortion (MTP)

Upto 12 weeks

surgical methods

Evacuation upto 6 weeks. This can be done using a menstrual regulation syringe (Karman's syringe)

- | | |
|---------------|--|
| 6 - 8 weeks - | Rapid dilatation using metal dilator under para cervical block followed by suction evacuation. |
| 8 - 12 weeks- | 2 stage dilatation using laminaria tent is done. Then suction evacuation is done. |

2nd trimester abortion

Best method is extra amniotic instillation of ethacridine lactate. This is a sterile solution of coloured dye. It is introduced into the uterine cavity extra amniotically through a foley's catheter. It acts by mechanical irritation. Can be followed by oxytocin drip.

16.5 VAGINITIS

Abnormal vaginal discharge is a very common symptom in the female. Excessive vaginal secretion is normal in the pre pubertal, ovulation time, premenstrual period and during pregnancy. This has to be differentiated from vaginal discharge due to infections.

Normal vaginal secretion is white in colour, odourless, and not associated with itching or soreness and will not contain any microorganism except doderleins bacilli. In the ovulation time the discharge is mucoid and colourless.

16.5.1 Monielial vaginitis

Caused by candida albicans - a fungus which thrive in acid pH. Hence common in pregnancy where vaginal pH is low. Also seen in diabetic woman. Can be transmitted to the sexual partner - also by contaminated water, towels etc. Also seen in patients taking antibiotics and steroids.

Diagnosis

Intense itching and discharge per vaginum. Discharge is curdy white and thick. The fungus can be demonstrated in the vaginal discharge by preparing a wet smear by adding one drop of saline to a little discharge and examining under the microscope.

Treatment

1. Local vaginal pessaries containing :

Nystatin - (10,000 units) clotrimazol - (100-200 mg), povidone iodine, miconazole

The pessaries are inserted for 3 - 6 consecutive days.

2. Oral: fluconazole - 150 mg - single dose
 ketoconazole - (200mg tab) 1 tab b.d. x 5 days
 Both partners should be treated.

16.5.2 Trichomonas vaginalis vaginitis

Caused by the protozoa trichomonas vaginalis.

Symptoms are intense itching and profuse foul smelling discharge p/v.

Treatment : metronidazole is the drug of choice.

200 mg thrice daily x 7 days for both partners.

Single dose of 2 g for both partners also can be given.

Tinidazole 2 g stat. also may be given.

16.5.3 Atrophic vaginitis

Occurs in the post menopausal women. This is due to oestrogen deficiency.

Malignancy should be excluded by a cervical smear (pap - smear)

Treatment

Local oestriol cream is applied 2 - 3 times daily until patient gets symptomatic relief.

16.6 CONTRACEPTIVES

16.6.1 Oral contraceptives

Combined pills having oestrogen and progestogens are usually used. The estrogen is ethinyl oestradiol 20/30 mcg. The progestogen is either norgestrel or desogestrel - 150 mg.

Tablets should be started from the 1st day of periods, continued for 21 days. The fresh packet should be taken exactly on the 7th day. Some OC pill packet have 7 placebo tablets of iron to be taken following the hormone tablets, so the patient need to remember just to take one tablet a day only.

Action

- | | |
|-------------|--|
| They act by | 1. inhibiting ovulation |
| | 2. act on the endometrium - causing atrophy. |

Contra indications

Thromboembolic disorders or history of thromboembolism, active liver disease, cancer of the genital tract or breast, avascular headache

16.6.2 Injectable contraceptives

Usually used on s are progesterone only Contraceptives like Depot Medroxyprogesterone acetate.

Dose: 150 mg

Given i.m. once in 3 months.

Action - like OC pills.

Contra indication

Active liver disease, malignancy of cervix or breast.

16.6.3 Emergency contraception

This is advised when the women had an unprotected coitus in the fertile period.

Methods

1. Oral administration of 2 tablets of combined OC pill (Ethnynl Estradol and Progesterone) as early as possible and then repeated after 12 hours.
2. Mifiprestone (Ru486). It is an ante progestin. 600 mg given i.m.
3. Post coital insertion of IUCD within 5 days.

16.7 DRUGS USED FOR INDUCTION OF OVULATION

Induction of ovulation is needed in treatment of infertility due to anovulation.

The usual drugs used are:

1. Clomiphen citrate
2. Gonadotrophins FSH & LH.

Clomiphene citrate

50 mg is given from the 3rd or 5th day of periods for 5 days. The dose may be increased upto 150mg/day

Complication is hyperstimulation and multiple ovulation resulting in multiple pregnancy.

Ideally patient should be monitored with serial ultrasound examination for evidence of ovulation and number of follicles.

Gonadotrophins

They are used when the patient fails to ovulate with clomiphene. Human menopausal gonadotrophin which has mainly the FSH activity is used for follicular growth. Human chorionic gonadotrophins which has the LH activity is used for inducing follicular rupture. 75 - 150 of HMG is given from 2nd or 3rd day of period. The follicular development should be watched by U.S.S examination. When the follicular size reaches 18 mm and oestradiol level is 200 pg, HCG is administered 5000 - 10,000 iu for follicular rupture. It is better that these drugs are used in bigger hospitals or infertility centres where there are facilities for monitoring the patients.

CHAPTER 17: ANTINEOPLASTIC AGENTS

Chemotherapy using various drug combinations is one of the modalities for treating malignant disease, the others include surgery and radiotherapy. Not all tumors can be treated by drugs, as the sensitivity to chemotherapy varies depending on the histological types.

Cytotoxic drugs can be classified as :

1. Alkylating drugs
2. Antimetabolites
3. Vinca Alkaloids
4. Cytotoxic Antibiotics
5. Hormones and antagonists
6. Miscellaneous agents

18.1 Alkylating Agents

Nitrogen mustards

Several drugs in this group are commonly used anticancer agents.

These are widely used anticancer drugs. They act by alkylating the DNA and thereby arresting cell replication. Mechlorethamine, cyclophosphamide, chlorambucil, melphalan, thiotepa, busulfan, procarbazine, carmustine, lomustine, senmustine and ifosfamide belong to this group.

Mechlorethamine(mustine hydrochloride)

It is a nitrogen mustard.

I : Disseminated Hodgkins disease, mycosis fungoides

C/I : Pregnancy

P/C : Being a vesicant drug, care should be taken to use gloves and to avoid contact with skin and eyes. It is given as i.v. infusion in to a fast flowing drip.

S/E : Leucopenia, thrombocytopenia, infection, bleeding, nausea, vomiting, sterility, skinrash, alopecia, hypersensitivity reaction, toxic encephalopathy, hypocalcemia, cardiac damage.

P/A : Injection 10 mg vial

Dose: 400 mcg/kg bw i.v. as rapid injection or infusion to a total dose of 8 mg in a single dose.

For local action in pleural or other malignancies it can be given

D/I : Aggravation of myelosuppressive activity when taken along with other myelosuppressive drugs.

Cost : Inj 10 mg (vial) Rs 113.00

Cyclophosphamide

I : Lymphomas, germ cell tumours, Sarcoma, multiple myeloma,

carcinoma of cervix, ovary, lung, breast, acute leukemia and several others.

C/I: Pregnancy and lactation, severe renal and hepatic failure, thrombocytopenia.

P/C: Renal failure. Dehydration should be avoided to minimize renal and vesical damage

S/E: Bonemarrow suppression, nausea, vomiting, alopecia, haemorrhagic cystitis, bladder carcinoma, bladder fibrosis, sterility foetal damage, cardiac damage, pulmonary fibrosis, fever, anaphylaxis, skin and nail hyperpigmentation, mucosal ulceration, liver damage, urticaria, transient cerebral symptoms, blurred vision.

P/A: Tablets 50 mg

Injection 100, 200, 500 mg, 1g.

Dose: Oral: 100-200 mg/kg bw to be given along with immunosuppressant drug.

Parenteral: 3-5 mg/kg bw to be given maximum in a single dose i.v. as push dose or as an i.v. infusion.

D/I: When given with other myelotoxic drugs or radiotherapy the combined adverse effects are increased

Cost: Tab 50 mg (50) Rs 110.00 - 115.00

Inj 100mg vial Rs 20.00

Chlorambucil

I: Chronic lymphatic leukaemia (CLL), lymphomas, multiple myeloma, macroglobulinemia, chorio carcinoma, testicular tumours and others.

C/I: Hypersensitivity, pregnancy, lactation.

P/C: Blood counts should be monitored every week.

S/E: Immunosuppression, myelosuppression, gastrointestinal symptoms, hepatotoxicity dermatitis, wasting syndrome.

P/A: Tablets 2mg, 4mg, 5 mg

Dose: 0.1 mg/kg/day for 3 to 6 weeks.

Maintenance dose - 2 mg daily.

D/I: Phenylbutazone and warfarin potentiate efficacy of chlorambucil

Cost: Tab 2mg (25) Rs 130.00

Melphalan

This is a phenylalanine mustard

I: Multiple myeloma, breast cancer, advanced ovarian carcinoma, malignant melanoma, polycythemic vera.

C/I: Hypersensitivity, pregnancy, lactation

P/C : Blood counts once a week at the initiation of therapy, later at longer intervals.

S/E : Nausea, allergic reactions, thrombocytopenia, bone marrow depression, inappropriate ADH secretion, amenorrhoea, leukemia, sterility, pulmonary infiltration.

P/A : Tablets 2mg, 5mg.
Injection 50 mg vial

Dose : 0.25 mg/kg/day \times 4 days repeated 4 - 6 weekly
Maintenance dose 1 - 4 mg/day.

D/I : Risk of renal failure with cyclosporine. Lung toxicity with carmustine. Renal dysfunction with cisplatin. With nalidixic acid allergic neurotic enterocolitis.

Cost :	Tab 2mg	(25)	Rs 193.00
	Inj 50 mg	vial	Rs 1520.00

Busulphan

I : Chronic myeloid leukaemia (CML), polycythemia vera, myelofibrosis, essential thrombocythemia.

C/I : Pregnancy, lactation.

P/C : Regular blood counts, hyperuricemia, second tumours such as acute leukaemia or carcinomas may occur on prolonged use.

S/E : Nausea, vomiting, pulmonary fibrosis, alopecia, generalised skin pigmentation, azoospermia, cataract, gynaecomastia, ovarian failure, leukaemia, hyperuricemia.

P/A : Tablets 0.5 mg, 2mg.

Dose : 2-8 mg oral daily as a single or divided doses till the leucocyte count falls below 10000. The drug is stopped and then restarted when the leucocyte count goes above 50000.

Note: Busulphan is seldom used as the primary treatment for CML at present due to severe irreversible long term damage and availability of better drugs like hydroxyurea. Busulphan used in doses of 1-4 mg/kg bw daily to ablate the host bone marrow before bone marrow transplantation.

Dacarbazine

I : Malignant melanoma, Hodgkins, Soft tissue sarcomas

C/I : Pregnancy, lactation, persons with severe myelosuppression.

P/C : Hepatic / renal impairment, haematologic monitoring, restrict food intake 4-6 hrs before therapy.

S/E : Nausea, vomiting, diarrhoea, anaphylaxis, bone marrow depression, urticaria, photosensitivity, hepatic necrosis, renal impairment, thrombocytopenia, blurred vision, flu-like syndrome, myalgia.

P/A: Injection 200mg vial

Dose: 2.5 - 4.5 mg/kg/day x 5-10 days

or

250 mg/m²/day x 5 days every 3 weeks

or

850mg/m² every 3-6 weeks given i.v.

D/I: Impairs the immunogenicity of the live attenuated vaccine. It forms precipitate with the hydrocortisone hemisuccinate.

Cost: Inj 200mg (vial) Rs. 415.00-521.00

Procarbazine

I: Hodgkins diseases, carcinoma of bronchus, brain tumour.

C/I, P/C: Hepatic and renal insufficiency, phaeochromocytoma, epilepsy, cardiovascular or cerebrovascular diseases.

S/E: Anorexia, nausea, vomiting, bone marrow suppression neurotoxicity psychosis depression, ataxia, orthostatic hypotension, skin rashes, pleuro pulmonary fibrosis, hepatic diseases, haemolytic anaemia

P/A: Capsules 50 mg

Dose: 100 - 200 mg/day orally to start with, later increased to 300 mg/day

D/I: MAO inhibitors potentiate neurotoxicity, phenolic compounds, alcohol, barbiturates and narcotics also increases neurotoxicity. Flushing syndrome with Alcohol.

Cost: Cap 50 mg Rs.0.00

Ifosfamide

I: Germ cell tumours, lymphomas, sarcomas, cervical, ovarian lung and breast cancer.

C/I: Thrombocytopenia, severe leucopenia, severe renal and hepatic impairment, pregnancy, lactation.

P/C: Hepatic and renal impairment, bone marrow suppression, dehydration.

S/E: Haemorrhagic cystitis, nausea, anorexia, hallucination, somnolence, confusion, leucopenia, immunosuppression, delayed wound healing.

P/A: Injection 1 g vial

Dose: 60mg/kg bw (upto 1.5 g/m² body surface) daily i.v. on 5 consecutive days. Attention should be paid to the specified doses of the relevant treatment regimen.

D/I: Additive bone marrow depression may occur with radiation therapy. There is adverse interaction with live and killed virus vaccines.

Cost: Inj 1 g (vial) Rs 297.00

17.2 Antimetabolites

These group of drugs interferes with different metabolic processes in the various parts of the cell and block cellular division. The group include methotrexate, mercaptopurine, thioguanine, 5- fluorouracil, cytarabine, 5-Azacytidine.

Methotrexate (MTX)

- I: Lymphoblastic leukemia, choriocarcinoma, hydatidiform mole, non-metastatic osteosarcoma and in small doses as immunosuppressant
- C/I: Severe hepatic or renal impairment, severe anaemia thrombocytopenia or leucopenia.
- P/C: Children, CNS disorders, GI disorders, bone marrow depression.
- S/E: Nausea, vomiting, diarrhoea, anaphylaxis, hepatic necrosis, fibrosis, renal toxicity, depigmentation.
- P/A: Tablets 2.5 mg, 5 mg
Injection 5mg, 15 mg, 50 mg ampoules.
- Dose: Leukemia
Maintenance Remission 30 mg/m² i.m. twice a week
Intrathecal dose 12 mg/m² (maximum 15 mg) dissolved in saline.
Choriocarcinoma 15 - 30 mg orally or i.m. x 5 days weekly repeated doses, 3-5 courses.
- D/I: Aminoglycosides decrease absorption and serum level of oral methotrexate. Charcoal reduces serum level of both oral and i.v. methotrexate. Etretinate cause hepatotoxicity. Folic acid or derivatives decrease response to methotrexate. NSAIDs increase plasma level of methotrexate. Serum concentration of phenytoin decreased. Probenecid, salicylates and sulfonamides increase efficacy and toxicity of methotrexate. Procarbazine increases nephrotoxicity of methotrexate. Serum levels of purinethol are increased. Asparaginase reduce toxicity. Food reduces the absorption of methotrxate when taken orally.
- Cost: Tab 2.5 mg (10) Rs 35.00
Inj 50 mg (ampoule) Rs 52.00- 93.00

Mercaptopurine

- I: In combination therapy for acute leukemia, chronic granulocytic leukemia.
- C/I: Breast feeding , pregnancy.
- P/C: Impaired renal or hepatic function, monitor uric acid level, blood counts, liver function test.
- S/E: Nausea, vomiting, diarrhoea, cholestasis bone marrow depression, pancreatitis oral and intestinal ulceration, hepatic necrosis.

P/A: Tablets 50 mg

Dose: 2-3 mg /kg/bw oral single or divided doses continuously.

D/I: Allopurinol delays catabolism of mercaptopurine resulting in severe toxicity. Other myelosuppressive agents enhance antineoplastic effect of mercaptopurine. Trimethoprim-sulfamethoxazole enhances bone marrow suppression.

Cost: Tab 50 mg (10) Rs 75.00

6 - Thioguanine

I: Combination therapy for AML

C/I: Drug toxicity and allergy

P/C: Renal dysfunction, hepatic dysfunction, renal dysfunction, hepatic veno occlusive disease.

S/E: Same as mercaptopurine. Drug toxicity.

P/A: Tablet 40 mg

Dose: Oral :2 mg/kg/day

D/I: Same as mercaptopurine

Cost: Tab 40 mg (25) Rs.976.00

5-Fluorouracil

I: Adjuvant in the treatment of carcinoma of breast, pancreas, urinary bladder, hepatoma, carcinoma of colon, and other parts of GI tract, premalignant keratosis of skin (topical treatment), multiple superficial basal cell carcinoma.

C/I: Serious infection, depressed bone marrow function.

P/C: Anemia, leucopenia, skin pigmentation, hepatic or renal impairment hypersensitivity.

S/E: Nausea, vomiting, diarrhoea, alopecia conjunctivitis, bone marrow depression, angina pectoris, cardiac arrhythmias, oral and GI ulcers, hyperpigmentation, chestpain, breathlessness.

P/A: Injection 250 mg, 500 mg ampoules,
Cream 5%

Dose: 12 mg/kg o.d. x 4 days i.v. (maximum 8000 mg)

If no toxicity 6 mg/kg on days 6, 8, 10, 12.

Maintenance 10 - 15 mg / kg/ week.

D/I: Cimetidine increases plasma concentration of 5-Fluorouracil. Other bone marrow depressants immunosuppressive agents, irradiation all lead to additive effect. With leucovorin, calcium toxicity of 5-fluorouracil increased. Enhanced toxicity with metronidazole. Elevation in alkaline phosphatase and transaminases, serum bilirubin

Cost: Not freely available

Cytarabine (cytosine arabinoside)

- I:** AML, ALL, CML blast phase, NHL in children
Treatment and maintenance of meningeal neoplasms, erythroleukemia.
- C/I:** Pregnancy, lactation
- P/C:** Monitor hepatic function, haematological parameters, uric acid levels, women of child bearing age, intrathecal administration in infants.
- S/E:** Leucopenia, anaemia, thrombocytopenia, reticulo cytopenia, GI disturbances, oral and anal ulcerations, hepatic and renal dysfunction, thrombophlebitis, peripheral neuro toxicity, high doses, rhabdomyolysis, conjunctivitis, anaphylaxis.
- P/A:** Injection 100 mg, 500 mg, 1000 mg vial
- Dose:** 100 mg/m² i.v. b.d. x 7 days.
- D/I:** Radiotherapy and other myelotoxic drugs potentiate myelotoxic effect. Increased serum levels of digoxin when concurrently used. Efficacy of both gentamicin and flucytosine is decreased.
- Cost:** Inj 500 mg vial .Rs. 475.00- 550.00

17.3 Vinca Alkaloids

The vinca alkaloids which are used mainly to treat acute leukemias, lymphomas and some solid tumors like breast and lung cancer. All the members of this has neurotoxicity which can produce peripheral or autonomous neuropathy. The members of this group include - Vincristine, vinblastine and vindesine.

Vinblastine

- I:** Hodgkin's disorders, non-Hodgkin's Lymphomas, mycosis fungoids, testicular cancer, kaposissarcoma
- C/I:** Leucopenia, bacterial infections, significant granulocytopenia.
- P/C:** Needle should be properly positioned in vein as leakage may cause considerable irritation.
- S/E:** Hepatic function impairment, leucopenia, azoospermia, nausea, vomiting, hypertension, alopecia.
- P/A:** Injection 10 mL vial
- Dose:** 3.7 mg/m² single dose increments at weekly interval maximum 18.5 mg/m².
- D/I:** Concurrent use with mitomycin cause acute shortness of breath and severe bronchospasm. Reduced plasma levels of phenytoin.

Concurrent use with erythromycin cause severe myalgia, neutropenia and constipation.

Cost : Inj 10 mL (vial) Rs.202.00

Vincristine

I : Acute leukaemia, lymphoma, neuroblastoma, Wilm's tumour.

C/I : Intrathecal administration, demyelinating Charcot - Marie disease, pregnancy, tooth syndrome.

P/C : Infection, neuromuscular disease, leucopenia, pulmonary diseases, leukaemia, radiation therapy, extravasation, concomitant neurotoxic drugs, eye contact, concurrent vaccination.

S/E : Local reaction if extravasation occurs, constipation, paralytic ileus, jaw pain, bone marrow depression, peripheral neuropathy, syndrome of inappropriate antidiuretic hormone (SIADH), breathlessness, hyper or hypotension.

P/A : Injection 1 mg, 5 mg ampoules.

Dose : 1.4 mg/m² weekly.

D/I : Decreased plasma digoxin level. Hepatic clearance of vincristine is reduced if L-asparaginase is administered first. So Vincristine should be given 12-24 hrs before L-asparaginase.

Acute pulmonary reaction may occur with mitomycin, reduced plasma phenytoin levels.

Cost : Injection 1 mg/mL (1mL) Rs.45.00 - 60.00

17.4 Cytotoxic Antibiotics

Antibiotics with cytotoxic properties is used widely in treating malignant diseases. The group includes doxorubicin, dactinorubicin, bleomycin, mithramycin, mitomycin, streptozocin, idarubicin and epirubicin.

Doxorubicin

I : GI tract carcinoma, AML, bronchogenic carcinoma, breast and ovarian carcinoma, soft tissue, and bone sarcoma, malignant lymphoma, non metastatic bladder carcinoma (intravesical), Wilm's tumour, neuroblastoma.

C/I : Buccal ulceration, bone marrow depression, pre existing heart disease, pregnancy.

P/C : Cardiac and hepatic dysfunction, haematological and cardiac monitoring, hyperuricemia infection.

S/E : Nausea, vomiting, diarrhoea, fever, red urine, ventricular arrhythmia, tissue damage on extravasation, cardiotoxicity, bone marrow depression, anorexia, stomatitis, alopecia, conjunctivitis.

P/A : Injection 10mg, 20mg, 50mg.

Dose : 60 - 75 mg/m² every 21 days or 30 mg/m² daily every 3 days
Repeat after 4 weeks. Maximum dose 550 mg/m².

D/I: Enhanced hepatotoxicity with mercaptopurine with cyclophosphamide - exacerbation of neurologic cystitis, increased clearance of doxorubicin with barbiturates, decreased serum level of digoxin. Increased toxicity of doxorubicin with streptozocin. Radiation induces damage to myocardium, mucosa, skin and liver increased.

Cost : Inj 50mg (vial) Rs.950.00 - 1200.00.

Daunorubicin

I: AML, ALL, disseminated neuroblastoma, Rhabdomyosarcoma.

C/I: Hypersensitivity, CHF, arrhythmias, bone marrow suppression, previous full cumulative dose of doxo or daunorubicin.

P/C: Cardiac, haematological monitoring, hepatic and renal impairment.

S/E: Nausea, vomiting, bone marrow depression, stomatitis, alopecia, rash, hyperpigmentation, cardiotoxicity, CHF, fever, chills, diarrhoea, local tissue damage, anaphylactical reaction, red urine.

P/A: Injection 20mg vial

Dose : 45 mg/m² on days 1,2,3.

D/I: Immunisation with live vaccine not recommended. Enhanced radiation toxicity.

Heparin, aluminium, dexamethazone are incompatible with daunorubicin.

Cost : Inj 20mg (vial) Rs.346.00

Bleomycin

I: Palliative and adjuvant to surgery and radiotherapy. Testicular tumour, squamous cell carcinoma of skin, neck and head, genito urinary tract, oesophagus, carcinoma of cervix, Hodgkin's and Non-Hodgkin's Lymphoma, choriocarcinoma, embryonal cell carcinoma of testis, brain tumour, glioma.

C/I: Pre existing pulmonary disease hypersensitivity.

P/C: Lymphoma patients, monitor pulmonary function, anaesthesia.

S/E: Nausea, vomiting, allergic reactions, fever, anaphylaxis, skin rashes, Raynaud's phenomenon, stomatitis, pulmonary fibrosis, hyperpigmentation, renal and hepatic toxicity.

P/A: Injection 15 mg, 30 mg vial.

Dose : 30 mg twice weekly

Total dose 300 - 400 mg

Small cell cancer - 0.25 mg - 0.5 mg / kg i.v., i.m., s.c. once or twice

weekly.

Hodgkins - 0.25 - 0.5 mg/kg i.v., i.m., s.c.

D/I: Digoxin and phenytoin levels decreased, increased radiation toxicity.
Oxygen increased pulmonary toxicity. Cisplatin toxicity increased.
Debilitation syndrome is seen with vincristine

Cost : Injection 15 mg (vial) Rs.950.00

Mitomycin

I: Adenocarcinoma, lymphosarcoma, seminoma, superficial bladder cancer, recurrent pterygium.

C/I: Haemorrhagic tendency, bonemarrow depression, thrombocytopenia. Should not be given i.m or s.c.

P/C: Leucopenia, oral ulcers, monitor renal and haematological status.

S/E: Leucopenia, thrombocytopaenia, pneumopathy, renal toxicity, stomatitis, thrombophlebitis, loss of appetite, nausea, vomiting, loss of hair, skin rash and possible haemolytic - uremic syndrome.

P/A: Injection 2 mg, 10mg vials

Dose : 6 - 10 mg i.v. twice weekly or 0.05 mg/kg/day x 5 days repeated after 2 days to a total dose of 60 - 100 mg.

D/I: Vinca alkaloids produce bronchospasm, bone marrow depression on radiation therapy, increased cardiotoxicity with doxorubicin, decreased antibody response to vaccines.

Cost : Injection 2 mg (vials) Rs. 77.00

Mithramycin (plicamycin)

I: Testicular tumour especially embryonal cell carcinoma, hypercalcemia.

C/I: Haemorrhagic diathesis.

P/C: Increased risk of bleeding even in minor surgeries

S/E: Haemorrhagic diathesis, arterial occlusion, malaise, fever, vomiting, skin eruptions, headache, apprehension, stomatitis, hypocalcemia, hepato renal dysfunction, disseminated intravascular coagulation.

P/A: Injection 2.5 mg

Dose : 25- 30 mcg/kg/day i.v. diluted in 1 L of 5% dextrose or saline and given over 4 - 6 hrs.

Hypercalcemia - 15 - 25 mcg/kg bw once in 4 - 7 days.

D/I: Increased risk of bleeding in patients on anticoagulant or thrombolytic agents or NSAIDs.

Decreased patient response to vaccines.

Mithramycin is seldom used as an anticancer agents. Not freely available.

Cost : Not freely available

17.5 Hormones and Hormonal Antagonists

Hormones and hormonal antagonists are successfully used to control cancers of the breast prostate and uterus and haematological and lymphoreticular malignancies. Most widely used among them are corticosteroids, androgens, oestrogens, antioestrogens, progestational agents and their analogues.

Stilboestrol

- I:** Disseminated mammary or prostatic cancer, menopausal disturbances.
- C/I:** Men with oestrogen dependant neoplasia, active thrombophlebitis, pregnancy and lactation.
- P/C:** Diabetes, hypertension.
- S/E:** Hepatic and cutaneous porphyria, erythema nodosum, erythema multiformae, feminisation.
- P/A:** Tablets 40mg, 80mg, 100mg, 250 mg.
Injection 250 mg, 5 mL ampoule.
- Dose:** 40 - 80 mg i.m. every 2 - 4 weeks i.v. initial treatment 500 mg in 5% dextrose subsequently 1 g/day in 1 hour x 5 - 10 days that 250 - 500 mg o.d or b.d.
Oral 50 mg t.d.s. increased to 200 mg t.d.s. maximum 1 g/day.
- D/I:** With bromocriptine amenorrhea, increases calcium absorption, increases therapeutic effects of glucocorticoids, increased risk of hepatotoxicity and nephrotoxicity with cyclosporine.
- Cost:** Tab 100mg (10) Rs. 85.00
Inj 250 mg (5 mL) Rs. 27.00

Ethinyl Estradiol

- I:** Disseminated carcinoma prostate or breast
- C/I:** Undiagonised vaginal bleeding, cardio or cerebro vascular thromboembolic disease, hypertension, hepatic impairment, porphyria, epilepsy.
- P/C:** Epilepsy, asthma, migraine, salt and fluid retension.
- S/E:** Gynaecomastia, decrease libido, hepatomas, epiphyseal fusion in children.
- P/A:** Tablets 0.01 mg, 0.02 mg, 0.05 mg, 1 mg.
- Dose:** 1 - 3 mg/day
Mainteneance 1 mg daily
- D/I:** With phenytoin enhanced efficacy and toxicity. Rifampicin increases oestrogen metabolism.
- With antihypertensives and anticoagulants reduced effect
- Cost:** Tab 0.1 mg (10) Rs. 10.00

Other preparations are not freely available.

Megesterol acetate

P/A: Medroxy progesterone acetate	Tablets :	2.5 mg, 10 mg
	Injection :	150 mg, 1mL vial
Hydroxy pregesteron caproate	Injection	250 mg/mL

Megesterol acetate

100 mg/day for breast cancer.

D/I: None reported.

Cost : Medroxy progesterone acetate

Tab 2.5 mg (10) Rs. 13.00 - 15.00

Inj 150 mg (1 mL) Rs. 150.00

Inj 250 mg (1 mL), Rs. 28.00 - 43.00

Hydroxy pregesterone caproate

Megesterol acetate

Tamoxifen

It is a non steroidal antioestrogen.

I: Advanced or metastatic carcinoma breast

C/I: Hypersensitivity, pregnancy

P/C: Premenopausal women

S/E: Nausea, vomiting, hot flushes, vaginal bleeding, dermatitis, pruritus, vulvae, menstrual irregularities.

P/A: Tablets 10 mg, 20 mg

Dose: 10 - 20 mg o.d.

D/I: Antagonism to the action of oral anticoagulants. Serum tamoxifen level is increased with bromocryptine. Cyclophosphamide level is increased.

Cost: Tab 10 mg (10) Rs. 16.00 - 52.00

Flutamide

It is an antiandrogen

I: Metastatic carcinoma prostate, hirsutism.

C/I: Severe chronic depression.

History of thromboembolism.

P/C: Liver Function Test (LFT) periodically, water retention.

S/E: Nausea, epigastric distension, vomiting, diarrhoea, gynaecomastia, galactorrhoea, hepatitis, breast tenderness, insomnia.

P/A: Tablets 250 mg

Dose: 250 mg t.d.s.

D/I: Enhances the effect of oral anticoagulants.

Cost: Tab 250 mg (10) Rs. 100.00 - 700.00

All Trans Retinoic Acid (ATRA)

I: M3 leukemia

S/E: ATRA syndrome, fever, chest pain, dyspnoea, pulmonary infiltration, hypoxemia.

ATRA syndrome (All Trans Retinoic Acid Syndrome): It occurs when ATRA is used for treatment of acute promyelocytic leukaemia (AML M₃). The most side effect of ATRA is ATRA syndrome. This is characterised by leukocytosis, pleural or pericardial effusion. Features of acute respiratory distress syndrome.

Corticosteroids

I: ALL, CLL, multiple myeloma, lymphoma, brain or spinal cord oedema, haemolytic anaemia, hypercalcemia, thrombocytopenia.

S/E: Sodium and water retention, hypokalemia, psychosis, diabetes mellitus, myopathy, osteoporosis, aseptic necrosis of bone, pancreatitis, peptic ulcer, pseudo tumor cerebri, glaucoma, cataract obesity, hyperlipidemia, non ketotic coma, immunosuppression, stress, impaired healing of wounds, growth failure amenorrhoea, suppression of pituitary.

D/I: Antitumour effects of 6-MP and cytarabine are inhibited by prednisolone.

17.6 Miscellaneous Agents

Several other drugs also used in cancer chemotherapy. These include hydroxy urea, mitotane, cisplatin, L-asparaginase, estramustin, epipodophyllin, etoposide, interferone, paclitaxel.

Hydroxy Urea

Drugs	Main Indication
Mitotane (O,P, DDD)	Inoperable Adrenocortical carcinoma, cushing's syndrome.
Cisplatin	Metastatic testicular and ovarian cancer, advanced bladder carcinoma, refractory squamous cell, neck and head carcinoma.
Carboplatin	First and second line therapy in ovarian carcinoma of epithelial origin.
L-Asparaginase	Malignant lymphoma, acute leukemia
Mitozantrone	CML, NHL, carcinoma of breast, ANLL,
Interferon Alpha - 2A	Hairy cell leukemia, Kaposi's sarcoma, CML
Paclitaxel	Metastatic ovarian and breast carcinoma.
Etoposide	Small cell lung cancer, acute monocytic and myelomonocytic leukemia, Hodgkins, non-Hodgkins Lymphoma, testicular tumor.

CHAPTER 18 : DRUGS USED IN ENT INFECTIONS

18.1 TOPICAL MEDICATION USED IN ENT PRACTICE

18.1.1 Nasal preparation

18.1.1.1 Local sympathomimetic decongestants

Action : Vasoconstriction of mucosal blood vessel when applied locally.

I: Allergic rhinitis, vasomotor rhinitis, sinusitis.

C/I: Glaucoma, rhinitis sicca, acute porphyria.

P/C: Prolonged use, pregnancy and lactation, hypotension, coronary artery disease, patients on monoamine oxidase inhibitors.

S/E: Slight tingling or burning sensation in nose, rebound nasal congestion.

P/A: **Ephedrine hydrochloride**

Nasal drops 0.5%, 0.75% w/v.

These can be prepared in the hospital pharmacy.

Oxymetazoline

Solution 0.01 %, 0.025%, 0.05% w/v.

Xylometazoline

Nasal drops 0.05%, 0.1% w/v

Phenylephrine hydrochloride

Nasal drops (combination) 0.25%, 0.5% w/v

Dose : 2-3 drops into each nostril every 8-12 h for 7 to 10 days.

Cost : **Ephedrine hydrochloride**

Nasal drops 0.75% w/v (10 mL) Rs. 6.00 - 7.00

Oxymetazoline

Solution 0.025% w/v (10mL) Rs. 17.00 - 18.00

Xylometazoline

Nasal drops 0.1% w/v (10 mL) Rs. 12.00 - 22.00

Phenylephrine hydrochloride

Nasal drops 0.25% w/v (10 mL) Rs. 12.00 - 14.00

Naphazoline hydrochloride

I: Decongesant.

C/I: Glaucoma, CV diseases, diabetes mellitus, hypertension, hyperthyroidism, hypersensitivity, pregnancy, lactation and children.

P/C: Stop medication and check with physician if changes in vision occur or if the condition worsens.

S/E: Hyperemia, dizziness, headache, increased sweating, nausea, nervousness, decrease in body temperature, weakness and drowsiness.

P/A: Nasal drops (combination) 0.025%, 0.05% w/v.

Dose: 1-2 drops into each nostril 3-4 times a day.

D/I: Pressor effect of naphazoline potentiated by TCAs or maprotiline.

Cost : Nasal drops 0.05% w/v (10 mL) Rs. 17.00 - 18.00

18.1.1.2 Corticosteroid nasal spray

Action : Suppress allergic reaction and reduce inflammation.

I: Seasonal and perennial allergic rhinitis, vasomotor rhinitis.

S/E: Candidiasis of nose.

P/A: **Beclomethasone**

Nasal spray 50 mcg/metered dose (md)

Budesonide

Nasal spray 50 mcg/md, 100 mcg/md

Dose : 1 - 2 sprays into each nostril b.d.

Cost : **Beclomethasone**

Nasal spray 50 mcg/md (200 md) Rs. 120.00 - 130.00

Budesonide

Nasal spray 50 mcg/md (200 md) Rs. 145.00 - 150.00

Nasal drops combinations containing hydrocortisone, naphazoline, betamethasone and neomycin are also available.

18.1.1.3 Mast cell stabilizers

Sodium cromoglycate

Action : Prevents allergic reactions by inhibiting the release of mediators of the allergic response from sensitised mast cells.

I: Allergic rhinitis.

P/A: Nasal spray 2%w/v

Dose : 1 spray into each nostril 4 - 6 times a day.

Coat : Nasal spray 2%w/v (20 mL) Rs. 20.00 - 74.00

18.1.2 Aural preparations

These include ear drops containing antibiotics, corticosteroids, antifungal agents and ceruminolytics.

18.1.2.1 Antibacterials

I: Chronic otitis media, otitis externa.

C/I: Allergy to the antibiotics.

18. Drugs Used in ENT Infections

P/C : Prolonged use should be avoided, aminoglycosides carry the risk of ototoxicity.

S/E : Meatal sensitivity, development of resistant flora, cochlear damage. On an average their use should be restricted to a total of 18 days.

P/A: **Chloramphenicol**

Solution 1%w/v

Ear drops 5%w/v

This causes skin sensitisation and therefore should be used only when definitely indicated.

Ciprofloxacin

Ear drops 0.3%w/v

Gentamicin

Ear drops 0.3% w/v

Norfloxacin

Ear drops 0.3% w/v

Dose : 2 - 3 drops 3 - 4 times daily.

Cost : **Chloramphenicol**

Solution 1%w/v (10 mL) Rs. 3.00 - 4.00

Ear drops 5%w/v (5 mL) Rs. 8.00 - 13.00

Ciprofloxacin

Ear drops 0.3%w/v (5 mL) Rs. 6.00 - 16.00

Gentamicin

Ear drops 0.3% w/v (5 mL) Rs. 5.00 - 8.00

Norfloxacin

Ear drops 0.3% w/v (5 mL) Rs. 8.00 - 12.00

18.1.2.2 Corticosteroids

Betamethasone

I : Eczematous inflammation, otitis externa.

C/I : Infection, hypersensitivity, pregnancy, laceration.

P/C : Avoid prolonged use.

P/A : Ear drops 0.1% w/v

Dose : 2 - 3 drops t.d.s.

Cost : Ear drops 0.1% w/v (5 mL) Rs. 7.00 - 13.00

In general corticosteroid ear drops are used in combination with antibiotics.

18.1.2.3 Antifungals

Clotrimazole

I: Otomycosis

S/E: Occasional skin irritation or sensitivity.

P/A: Ear drops 1%w/v

Dose: 4 - 5 drops t.d.s. or q.d.s.

Cost: Ear drops 1% w/v (10) Rs. 11.00 - 16.00

Combination of antibiotics, corticosteroids and antifungal agents are also available as ear drops.

18.1.2.4 Ceruminolytics

Action: Softening of ear wax.

I: Hard wax filling external auditory canal.

P/A: Sodium bicarbonate (5% w/v)

Docusate sodium (5% w/v)

Cost: Docusate sodium Ear drops 5% w/v (10 mL) Rs. 13.00 - 14.00

Local preparation of ear drops

Sodium bicarbonate 5g

Glycerol 30 mL add distilled water to 100 mL. To be used 3-4 times daily.

This is cheap and easily prepared. Hence this is better for wider use.

18.1.3 Oropharyngeal preparations

18.1.3.1 Anti inflammatory analgesics

I: Painful inflammatory condition of oral cavity and oropharyngeal.

P/A: Benzydamine hydrochloride Solution 15%w/v (120, 200 mL)

Choline salicylate Oral gel 8.7% (10, 15 g)

Dose: Benzydamine hydrochloride Solution - gargle 15 mL every 3-4 h.

Choline salicylate Gel - apply 1 - 2 drops over affected area 3 - 4 times a day.

Cost: Benzydamine hydrochloride Solution 15%w/v (120mL)
Rs. 24.00 - 25.00

Choline salicylate Oral gel 8.7% (15 g) Rs. 18.00 - 20.00

18.1.3.2 Antibacterials

I: Infections of the mouth and gums, gingivitis, pyorrhoea, stomatitis, oral ulcers, adjuvant in treatment of pharyngitis and tonsillitis.

P/A: Chlorhexidine Solution 0.2% w/v

Chlorxylenol Solution 1.02% w/v

18. Drugs Used in ENT Infections

Povidone iodine	Soluton	1% w/v
Metronidazole	Gel	
Dequalinium chloride	Lozenges	250 mcg

Dose : Chlorhexidine solution - 10 mL to be rinsed b.d., keep atleast 1 min in the mouth.

Chlorxylenol solution - dilute with water and rinse or garle as required.

Povidone iodine soluiton - garle undiluted or diluted with equal quantity of water for 30 seconds q.d.s.

Metronidazole gel - to be applied for 15 minutes b.d.

Dequalinium chloride lozenges - to be taken t.d.s.

Cost : Chlorhexidine Solution 0.2% w/v (100 mL) Rs. 26.00 -28.00

Chlorxylenol Solution 1.02% w/v(50 mL) Rs. 6.00 - 8.00

Povidone iodineSoluton 1% w/v (50 mL) Rs. 12.00 - 18.00

18.1.3.3 Antifungal preparations

Clotrimazole

I: Fungal infection of oral cavity.

P/A: Mouth paint 1% w/v

Dose : 10 - 20 drops applied over the affected part in the mouth 3 - 4 times daily.

Cost : Mouth paint 1% w/v (15 mL) Rs. 16.00 - 18.00

18.2 SYSTEMIC ANTIHISTAMINES

Chlorpheniramine Maleate

I: Allergic rhinitis, acute and chronic urticaria, atopic dermatitis, angioneurotic oedema.

Dose: Adults - 4 mg t.d.s or q.d.s.

Children - 6-12 years: 5 mL t.d.s. (Syrup 0.5 mg/5 mL)

Children - 1-5 years: 2.5-5 mL t.d.s.

Children - upto 1 year: 2.5 mL t.d.s.

Cetirizine

Highly selective Histamine H₁ receptor antagonist. No effect at serotonergic, muscarinic, dopeminergetic D₂ and alpha adrenergic receptors. No effect at calcium channel and H₂ receptors.

I: Allergic rhinitis, chronic urticaria, allergic conjuntivitis, atopic dermatitis, pruritus, adjunct in asthma management.

C/I: Hypersensitivity to the drug, lactation.

P/C: Pregnancy, renal impairment, elderly.

S/E: Mild and transient side effects such as headache, drowsiness,

agitation, dry mouth, G.I. discomfort.

P/A: Tablet 5 mg, 10 mg (10)

Syrup 1 mg/1 mL (30, 50, 60mL)

Dose: Adults - 10 mg once or b.d.

Children - 6 - 12 years - 5 mg o.d.

Children 2 - 5 years - 2.5 - 5 g o.d.

D/I: Alcohol may potentiate CNS depression.

Cost: Tab 5 mg, 10 mg (10) Rs. 7.00 - 28.00

Syrup 1 mg/1 mL (60 mL) Rs. 19.00 - 26.00

Astemizole

Long acting sedative histamine H₁ receptor antagonist, does not readily cross the blood brain barrier, less sedation and less psychomotor impairment.

I: Allergic rhinitis, allergic conjunctivitis, chronic urticaria and other allergic conditions.

C/I: Pregnancy, lactation, concomitant use of macrolides, ketoconazole and itraconazole.

P/C: Hepatic impairment, QT prolongation, ventricular arrhythmias, electrolyte disturbances.

S/E: Occasional weight gain, ventricular arrhythmias, QT prolongation, electrolyte disturbances, drowsiness, headache, dry mouth.

P/A: Tablet 10 mg

Syrup 1 mg/mL (10, 30, 60 mL)

Dose: Adults - 10 mg o.d.

Children - 6 -12 years - 5 mg o.d.

Children - 2 - 6 yrs - 1 mg/5 kg/day.

D/I: Ketoconazole, itraconazole, erythromycin, antiarrhythmic agents, neurolytics, tricyclic antidepressants and diuretics cause severe CVS defects. Potentiates MAOIs, alcohol and CNS depressants.

Cost: Tab 10 mg (10) Rs. 10.00 - 20.00

Syrup 1 mg/mL (60 mL) Rs. 10.00 - 28.00

Azatadine Maleate

Histamine H₁ receptor blocker with antiserotonin, anticholinergic and sedative properties.

I: Allergic rhinitis, chronic urticaria.

C/I: Pyloric stenosis complicating ulcer, prostatic hypertrophy, urinary retention, glaucoma, pregnancy, lactation, patient recurring MAO inhibitor therapy.

P/C: Hypertension, hyperthyroidism.

S/E: Drowsiness, gastritis, headache, blood dyscrasias.

P/A: Tablet 1 mg
Syrup 0.5 mg/5mL

Dose: Adults - 1-2 years b.d.
Children 6 -12 yrs 1/2 to 1 mg b.d.
Children 1 - 5 years : 1/4 - 1/2 mg b.d.

D/I: MAO inhibitors enhance anticholinergic side effects, enhances sedative drugs, potentiates CNS depression with alcohol and other CNS depressants drugs.

Cost :	Tab	1 mg	(10)	Rs. 23.00 - 24.00
	Syrup	0.5 mg/5 mL	(50 mL)	Rs. 25.00 - 26.00

Clemastine

Potent histamine H₁ receptor antagonist, does not readily cross blood-brain barrier.

I: Allergic rhinitis, urticaria, itching, dermatosis, drug eruptions, pruritus, contact dermatitis, adjunct in chronic eczema, insect bites and stings.

C/I: Glaucoma, prostatic enlargement, peptic ulcer, hypersensitivity

P/C: Bronchial asthma, emphysema, pregnancy, lactation

S/E: Sedation, dizziness, dry mouth

P/A: Tablet 1 mg
Syrup 0.5 mg/5 mL

Dose: Adults and children >12 years: 1 mg b.d.
Children 6-12 years: 0.5-1 mg b.d.
Children 3-6 years: 5 mL b.d.
Children 1-3 years: 2.5-5 mL b.d.
Children upto 1 year: 1-2.5 mL b.d.

D/I: Enhances the effect of sedatives, hypnotics, alcohol, MAO inhibitors.

Cost:	Tab	1 mg	(6)	Rs. 25.00 - 35.00
	Syrup	0.5 mg/5 mL	(50 mL)	Rs. 37.00 - 40.00

Cyproheptadine

Dimethindene maleate

Classical histamine H₁ receptor antagonist, has same antagonistic action at muscarinic and serotonin receptors, has good antipruritic action.

I: Pruritus of any aetiology, allergic rhinitis, urticaria, drug and food allergies.

C/I: Neonates and infants, urinary retention.

P/C: Elderly, glaucoma, prostrate hypertrophy, epilepsy.

S/E: Urinary retention, constipation, tachycardia, arrhythmias, GI upsets, sedation.

P/A: Tablets 1 mg, 2.5 mg

Dose: Adult - 1 to 2 mg t.d.s.

Children < 6 years - 0.5 mg t.d.s.

D/I: Effect of sedatives, phenytoin and anticholinergic drugs enhanced on concurrent use.

Cost: Tab 1 mg (100) Rs. 135.00 - 140.00

Diphenhydramine (see section 15.1,7)

Embramine

Classical antihistamine

I: All allergic conditions

C/I: Neonates, infants, urinary and GI obstruction, paralytic ileus

P/C: Elderly, epilepsy, glaucoma, BPH, CVS diseases.

S/E: Tinnitus, vertigo, nausea, headache, arrhythmias, blood dyscrasias, hypotension.

P/A: Tablet 25 mg

Dose: 25-50 mg o.d.

D/I: Enhances CNS depression produced by sedatives, alcohol, barbiturates, hypnotics and neuroleptics. Additive antimuscarinic effect with MAOIs, atropine and TCAs. Masks ototoxicity due to aminoglycosides.

Cost: Tab 25 mg (10) Rs. 13.00 - 14.00

Fexofenadine

Nonsedating antihistamine - selective peripheral H₁-receptor antagonist.

I: Allergic rhinitis, chronic idiopathic urticaria

C/I: Hypersensitivity, lactation

P/C: Renal and hepatic impairment, pregnancy

S/E: Drowsiness, headache, nausea, leucopenia

P/A: Tablet 120 mg, 180 mg

Dose: Allergic rhinitis - 120 mg/day

Chronic idiopathic urticaria - 180 mg/day

D/I: Erythromycin and ketoconazole increases plasma concentration of the drug.

Cost: Tab 120 mg (10) Rs. 4.00

Hydroxyzine

It has both antianxiety and antihistaminic activity

I: Pruritus, acute and chronic urticaria and dermatosis, anxiety

C/I: Pregnancy, neonates, urinary and GI obstruction.

P/C: Renal impairment, lactation, peptic ulcer, BPH.

S/E: Tachycardia, arrhythmias, headache, blood dyscrasias, tinnitus

P/A: Tablet 10 mg, 25 mg

Syrup 10 mg/5 mL

Injection 25 mg/mL

Cost: Tablet 25 mg (10) Rs. 9.00 - 10.00

Syrup 10 mg/5 mL (100 mL) Rs. 24.00 - 25.00

Injection 25 mg/mL (2 mL) Rs. 6.00 - 7.00

Loratidine (see section 6.1.2.3)

Methdilazine

Classical antihistamine with anticholinergic, antiserotonergic and central sedative effects.

I: Hypersensitivity reactions, pruritic skin lesions, migraine prophylaxis.

C/I: Neonates, glaucoma, GI obstruction, urinary obstruction, paralytic ileus.

P/C: Elderly, peptic ulcer, epilepsy, severe CVS disease, BPH, pregnancy, lactation.

S/E: Sedation, hypotension, headache, arrhythmias, blood dyscrasias, urinary retention.

P/A: Tablet 8 mg

Syrup 4 mg/5 mL

Dose: 8 mg 2-4 times daily.

D/I: Enhances CNS depression produced by sedatives, alcohol, barbiturates, hypnotics and neuroleptics. Additive antimuscarinic effect with MAOIs, atropine and TCAs. Masks ototoxicity due to aminoglycosides.

Cost: Tablet 8 mg (10) Rs. 7.00 - 8.00

Syrup 4 mg/5 mL (115 mL) Rs. 17.00 - 18.00

Pheniramine maleate (see section 15.1.7)

Promethazine (see section 11.5.4)

Terfenadine

Tripolidine

Classical antihistamine

I: Hay fever, respiratory disorders of allergic nature, allergic dermatosis, urticaria, angiomatous oedema, pruritus.

C/I: Hypersensitivity, severe renal and hepatic dysfunction.

P/C: Should not drive or operate machinery while on medication.

S/E: Drowsiness, skin eruptions

P/A: Syrup 1.25 mg/5 mL

Dose: 2.5 mg 4-6 h.

D/I: Enhanced effect with concurrent use of CNS depressants and alcohol.

CHAPTER 19 : DRUGS USED IN OPHTHALMOLOGY

Topical preparations directly applied to the eye constitute a major proportion of the drug armamentarium used in ophthalmological practice. In addition, systemic administration of several groups of drugs such as anti-infective agents, corticosteroids, non-steroidal antiinflammatory drugs, antihistamines, immunomodulators, vitamins, analgesics and others are used from time to time frequently.

19.1 ROUTES OF ADMINISTRATION OF DRUG

1. Topical application - applied over the eye directly.
 - a. Eye drops - well absorbed, blurring of vision is minimal, on prolonged and repeated use systemic effects may occur. The optimum volume to be used each time is 20 microlitre.
 - b. Ointments - They stay longer over the cornea and conjunctiva, they are not diluted freely by tears, they are not readily drained into the nasolacrimal system. Blurring of vision and stickiness of the eye are relative disadvantages. Drugs such as antibacterials are preferably given as ointments if a prolonged contact time is desired.
 - c. Inserts - These are soluble drugs incorporated in polymer gels - (eg : gelatin wafers) and introduced into the eye.
 - d. Iontophoresis- This is the method by which the drug is introduced into the eye with the help of electromotive force. It is only seldom used.
 - e. Through hydrophylic (soft) contact lenses :
Specially designed soft contact lenses impregnated with the drug releases the medication for prolonged periods upto several hours. This is used under special circumstances. eg . pilocarpine, gentamicin.
2. Subconjunctival injections :
Injections are made either below the conjunctiva or below tenon fascia. After subconjunctival injection the drugs stays longer at the site, and a part of it also leaks into the conjunctival sac. Subtenon injection leads to better absorption of the drug.
3. Anterior and posterior subtenon injections.
4. Retrobulbar injections :
Used for anaesthetising the eye before surgery, and for delivering drugs such as corticosteroids in optic neuritis, retrobulbar neuritis, etc. Injections are done with 25 gauge needle 40 mm long.
5. Intracameral injection
This is the administration of drug into the anterior chamber

6. Intravitreal injection

Direct introduction of the drug into the vitreous as in endophthalmitis.

19.2 Antibacterial agents

Almost all the available antibacterial agents are used from time to time. The general principles to be followed in their use are to be adhered to. Common indications include infective blepharitis, conjunctivitis, gonococcal ophthalmitis, dacryocystitis, panophthalmitis, orbital cellulitis, corneal ulcers and all other bacterial diseases. They can be used topically and also systemically.

Strength of commonly used antibiotic eye drops for instillation into the eye

Penicillin G	10,000 units / mL
Bacitracin	10,000 units / mL
Gentamicin	9.1 mg/mL
Tobramycin	9.1 mg/mL
Carbinicillin	4 mg/mL
Cephazolin	33 mg/mL
Chloramphenicol	0.5%
Norfloxacin	0.3 %
Ciprofloxacin	0.3 %
Framycetin	0.5 %
Sulphacetamide	10, 20 and 30 %

Antibacterial ointments for topical use

Chloramphenicol applicaps	1 %
Gentamicin	0.3 %
Tetracycline HCl	1 %
Oxytetracycline HCl	1 %
Framycetin	0.5%
Neomycin +	1700 iu +
Polymyxin B +	5000 iu +
Gramicidin	0.025 mg
} per gram	
Norfloxacin	0.3 %
Ciprofloxacin	0.3 %

19.3 Antiviral agents**Idoxuridine**

Used in herpes simplex and vaccinia keratitis

S/E: Irritation, oedema, punctal closure, ptosis.

P/A: Solution 0.1 %

Ointment 0.5 %

Dose : One drop instilled hourly during day and 2 h during night

Trifluridine

Action and use similar to idoxuridine

P/A : Solution 1 %

Dose : 1 drop hourly during day and 2 h during night for 7 days.

Adenine arabinoside (vidarabine)

Used in viral keratitis and uveitis caused by HSV

S/E : Irritation, allergy.

P/A : Ointment 3 %

Dose : 4 to 5 times daily for 7 days .

Acyclovir

Reaches adequate concentration in aqueous. Less toxic, wide spectrum against lesions caused by HSV, VZV, EB virus, CMV.

P/A : Eye ointment 3 %

Cream 5 %

Dose : Apply 5 times/day till lesions heal.

Systemic therapy is also necessary.

Along with the antiviral medication corticosteroid therapy may be required in lesions caused by herpes viruses.

19.4 Antifungal agents

Amphotericin B

Dose : Topical use - 0.1 to 0.2 % solution hourly.

Subconjunctival injection - 2 to 5 mg in 0.5 mL

Anterior chamber irrigation - 500 mcg in 0.1 mL

Intravitreal injection - 5 mcg in 0.1 mL

Nystatin

P/A : Occular cream - 3.3 % (1 lakh unit/g)

Occular ointment - 3.3 % (1 lakh unit/g)

Occular suspension - 1 lakh unit/mL.

Clotrimazole

P/A : Drops 1 % in arachis oil

Dose : Every hour till response occurs, then q.d.s. for 8 - 12 weeks

Miconazole

P/A : Drops 1 % in arachis oil

Cream 2 %

Dose : Every hour during day and 2 h during night.

Econazole

P/A: Solution 1 %

Dose : Every hour during day and 2 h during night.

Ketoconazole

P/A: Drops 1 % in arachis oil

Dose : Every hour during day and 2 h during night.

19.5 Local anaesthetics

Xylocaine

P/A: Drops 4%

19.6 DRUGS USED IN MEDICAL MANAGEMENT OF GLAUCOMA

At present diagnosis of glaucoma, its medical and surgical management and preventive measures have all reached a high degree of advancement and sophistication. The ophthalmologist has a wide range of therapeutic modalities.

Most of the antiglaucoma drugs are administered topically. Medication is tried first in one eye and if found to be safe and effective it is extended to the other eye also.

19.6.1 Cholinergic drugs used topically

Drug	Mechanism of action	Strength % solution	Duration of action	Frequency of administration
Pilocarpine	Parasympathomimetics	0.25-10	4-8 hr	b.d.- q.d.s.
Methacholine	"	2-20	1-12 hr	b.d.- q.d.s.
Carbochol	"	0.75-3	4-12 hr	t.d.s.
Aceclidine	"	0.5-4	4 - 8 hr	q.d.s.
Physostigmine	Inhibition of choline esterase	0.25-1 0.25-0.5 oint	4-6 hr	q.d.s.
Neostigmine	"	3-5	4-6 hr	q.d.s.
Isoflurophate	"	0.25 oint	12 hr-7 days	o.d.
Demecarium bromide	"	0.125-0.25	12 hr-7 days	o.d.
Echothiophate iodide	"	0.03-0.25	12 hr-7 days	o.d.

S/E: Pilocarpine is well tolerated, blurring of vision and temporary

myopia may develop, periorbital pain, ocular muscle spasm, allergy, band keratopathy, ciliary muscle spasm, uveitis, cataract, detachment of retina, vitreous haemorrhage, mild parasympathomimetic systemic effects.

Alternatively, pilocarpine can also be administered as a gel, through soft contact lenses or as an ocular insert (ocuser).

19.6.2 Adrenergic drugs

Drugs acting on the adrenergic system are also used in the management of glaucoma. They alter the dynamics of aqueous humour as given below.

Agonists

- Beta2 agonists
 - increases trabecular flow
 - reduces the formation of aqueous humour.
- Alpha1 and Alpha2 agonists - reduces the formation of aqueous humour.

Antagonists

- Beta2 antagonists - reduces the formation of aqueous humour.
- Alpha1 and Alpha2 antagonists - reduces the formation of aqueous humour.
- increases the outflow.

Epinephrine

Stimulates alpha and beta receptors. Action starts in 1 hour and is maximal in 2 - 6 hours and lasts for 12 - 24 hours.

C/I: Systemic hypertension, cardiac failure, thyrotoxicosis

S/E: Systemic effects, local irritation, allergy

P/A: Solution 0.5 %, 1 % and 2 %

Epinephrine polymeric matrix releases the drug slowly over 12 hrs at the rate of 1-4 mg/hour.

Timolol

Beta1 and Beta2 antagonists. Intraocular pressure starts falling in 30 minutes and action lasts for 24 - 48 hours. The initial beneficial effect starts falling in a few weeks.

P/A: Solution 0.25 % and 0.5 %

Dose: to be used b.d.

Betaxolol

Beta1 antagonist. Reaches high concentration in ciliary epithelium.

P/A: Solution 0.5 %

Dose: Applied b.d.

Levobutanol

Non selective Beta2 antagonists.

P/A: 0.5% Solution applied o.d. or b.d.

19.6.3 Systemic drugs used in glaucoma

Acetazolamide

Carbonic anhydrase inhibitor

Hyperosmotic agents

Oral glycerol - 1.5 to 3 mL/kg bw as 50% solution

Isosorbide dinitrate - 1.5 to 4 mL/kg bw of 45% solution.

Ethyl alcohol - 2 to 3 mL/kg bw as 40-50 % solution..

Intravenous mannitol - 2.5 to 7 mL/kg bw of 20 % solution i.v.

Urea - 30 % solution given i.v. in a dose of 2 to 7 mL/kg slowly.

C/I: Renal failure.

S/E: Rebound rise in intraocular tension, thrombophlebitis, general pain at the site of injection, urticaria, anaphylaxis, fever, laryngeal oedema. Gastrointestinal - nausea, vomiting, diarrhoea and cramps
CVS - angina, cardiac failure, pulmonary oedema;

CNS - headache, confusion, delirium;

Renal - diuresis, loss of potassium, prostatic symptoms,

19.7 CORTICOSTEROIDS USED IN OPHTHALMOLOGY

Systemic administration is needed in several conditions and these follow the same guidelines for systemic therapy in other conditions.

Topical corticosteroids are employed for several allergic and inflammatory lesions where immunosuppression and antiinflammatory actions are desirable.

I: Contact dermatitis of lids, allergic lesions of the eyes, phlycten, ocular pemphigus, Mooren's ulcer, keratitis, corneal burns, iritis, iridocyclitis, posterior uveitis, optic neuritis, retrobulbar neuritis, endocrine exophthalmos, postoperative states.

C/I: Local and systemic infection. *See individual sections.*

S/E: Glaucoma, cataract, xerophthalmia, ptosis, mydriasis, allergic keratitis, infections by bacteria and fungi, and rarely systemic side effects.

P/A: **Cortisone**

Suspension 0.5 %

Ointment 1.5 %

Hydrocortisone

Suspension 0.5 %

Ointment 1.5 %

Solution 0.2 %

Prednisolone

Ointment 0.2 %

Solution 0.5 %

19. Drugs Used in Ophthalmology

Dexamethosone

Ointment	0.5 %
Solution	0.1 %

Betamethasone

Ointment	0.5 %
Solution	0.1 %

Fluomethalone

Suspension	0.1 %
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Triamcinolone

Ointment	0.1 %
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Hydroxymethyl progesterone

Suspension	1 %
Ointment	0.1 %

Dose : Depends on the clinical indication.

Drop 2 - 3 times daily or even more frequently.

Injections into the eye - subconjunctival, anterior and posterior subtenon and retrobulbar - are done in different indications.

All the NSAIDs can be used to suppress inflammation and give pain relief as per the guidelines.

Allergic conditions demand the administration of **systemic antihistamines**.

Anticancer drugs are indicated in several neoplastic conditions of the ocular structures.

19.8 MYDRIATICS, MIOTICS AND CYCLOPLEGIC DRUGS

These are commonly used in day to day ophthalmological practice.

A. Parasympatholytic drugs

Atropine, homatropine, scopolamine, cyclopentolate, tropicamide, oxyphenonium.

B. Sympathomimetic drugs

Direct acting, i.e. acting directly on muscle end plate. eg: epinephrine (adrenaline) and phenylephrine.

Indirect acting, i.e. acting by interfering with the natural neuromuscular effector agent. eg: hydroxyamphetamine, cocaine, ephedrine.

Atropine sulphate

Mydriatic and cycloplegic, action lasts for 2 weeks.

I : Iritis - to allay pain, prevent synechiae, give rest to the muscles.

Glaucoma - to produce ciliary block.

Intraocular surgery - pre and post-operatively.

C/I: Narrow angle glaucoma, allergy.

P/C: Avoid atropine drops in children due to risk of systemic absorption. In them ointment is preferred.

S/E: Contact dermatitis, xerostomia, flushing of skin and delirium.

P/A: Solution 0.5 % - 4 % (most commonly used is 1 % solution)

Ointment 0.3, 0.4 and 0.6 mg/mL.

Injection 0.3, 0.4 and 0.6 mg/mL.

Homatropine

Synthetic alkaloid similar in action to atropine, but weaker and of shorter duration (1 to 2 days).

I: Refraction, postoperatively to relieve spasm, uveitis.

P/A: Solution 2 %

Cyclopentolate

Action starts within 20 - 45 min and it lasts for 12 - 24 hours.

I: Refraction, ciliary spasm, postoperative state, iridocyclitis.

C/I: Narrow angle glaucoma.

S/E: Visual hallucination, incoherence of speech.

P/A: Ointment 1 %, 2 %

Tropicamide

Rapid action, onset of action within 15 min and it last for upto 2 hours.

I: Refraction, fundus examination and fundus photography.

P/A: Drops 0.5 %, 1 %.

Epinephrine (see section 19.6.2)

Phenylephrine

Produces mydriasis without cycloplegia. Effects occur within 30 min and lasts for 2 - 3 hours.

I: For fundoscopy, preoperatively, malignant glaucoma.

C/I: New born infants cardiac failure.

P/A: Solution 5 %, 10 %

D/I: Morphine, guanethedine, tricyclic antidepressants.

Cocaine

Indirectly acting adrenergic drug to be used for local anaesthesia and mydriasis.

19.9 DYES USED IN OPHTHALMOLOGY

Fluorescein Sodium

This is used to detect breaks in the corneal epithelium. Intact epithelium resists the penetration of this dye. When there is disruption of the epithelium, the cornea gets stained.

I : To detect corneal ulcers, fundus fluorescein angiography.

P/C : Cross infection may develop due to contamination of the eye drops. This is avoided by using

1 : 25,000 phenyl mercuric nitrate as the preservative.

S/E : Yellow discolouration of urine and skin (after i.v. use) for upto 24 hours. False positive Benedict's test in urine. Dyschromatopsia. Systemic effects like allergy, hypotension and shock. Iatrogenic infection of the eye.

P/A: For i.v. use	Solution	1 %, 5 %, 25 %
Topical use	Solution	2 %

Dose : Not to exceed 15 mg/kg bw.

19.10 NUTRITIONAL DISORDERS AFFECTING THE EYE

Vitamin A deficiency

Night blindness, Bitot's spots, corneal ulceration, xerophthalmia, keratomalacia, blindness.

Recommended dose of Vitamin A is 2,00,000 units daily for 2 days orally once in 6 months, or 1,00,000 unit i.m. injection.

Thiamine deficiency, niacin deficiency, riboflavin deficiency, pyridoxine deficiency, Vitamin B12 deficiency, biotin deficiency and Vitamin C deficiency also cause nutritional disorder of the eye.

Appendix

Drugs which are particularly prone to cause ocular toxicity

Antibacterials - chloramphenicol, ethambutol, isoniazid, nalidixic acid, rifampicin, griseofulvin, chloroquine, quinine

NSAIDs

Cardiovascular drugs - amiodarone, digoxin, quinidine

Drugs acting on the nervous system - anticonvulsants (phenytoin), antidepressants, antiparkinsonism drugs, hypnotics, tranquilizers, ethyl alcohol, methyl alcohol, anticancer drugs

Miscellaneous - continuous oxygen in infants, tobacco, excess Vitamin A and Vitamin D.

Addendum of Chapter-3

Drug used in Gastro Intestinal Disorders

3.11.3 Drug management of haematemesis

Selection of the drug depends upon the cause of haematemesis

Antacids

Antacids in a dose of 4 teaspoonful 2h is recommended

H₂ receptor blocking drugs

Cimetidine (See section 3.2)

Ranitidine (See section 3.2)

Famotidine (See section 3.2)

Proton pump inhibitors

Omeprazole (See section 3.2.2)

Lansoprazole (See section 3.2.2)

3.11.4 Drugs which lower portal pressure

Propranolol (beta adrenergic blockers) (see also section 5.7.3)

Dose: 40 mg b.d. increased to 80 mg b.d. (maximum 160 mg b.d.)

Vasopressin and its analogues (see also section 7.2.2.2)

Somatostatin

3.11.5 Drugs with primary biliary cirrhosis

Immunosuppressants

Azathioprine (See section 8.2.3)

Urso deoxycholic acid (See section 3.11.2)

3.11.6 Wilson's disease

Copper chelating agents

D-penicillamine (See section 8.2.3)

3.11.7 Haemochromatosis

Iron chelating agents

Desferrioxamine (See section 9.5)

Deferiprone (See section 9.5)

PART - II

**Guidelines
for
Clinical Management
at the
Peripheral Hospitals**

1. GENERAL CONDITIONS

1.1 HYPERPYREXIA

Hyperpyrexia may be due to a variety of clinical conditions, the commonest cause in our state being viral fever. Even though the term hyperpyrexia denotes the clinical state with temperature above 106°F (41°C), any state of fever with temperature above 102°F (39°C) will make the patient very uncomfortable and require emergency treatment. Irrespective of the cause of pyrexia, general measures to reduce the temperature are to be undertaken urgently. Patients must be given tepid sponging with cold water and a dose of 1 g paracetamol to be given orally or 300 mg i.m., as an antipyretic. If not responding, a dose of 25 mg of chlorpromazine i.m. may be useful. The definite treatment depends on the underlying cause which may vary from viral fever, leptospiral illness, pneumonia, enteric fever or cerebral malaria. Once the temperature is brought down by tepid sponging and antipyretics, investigations to find out the aetiology must be commenced.

1.2 ENTERIC FEVER

Enteric fever is suspected when there is prolonged fever with coated tongue, soft splenomegaly, absence of leucytosis and rising titres of antibodies to 'O' antigen in widal tests. The disease can be confirmed by blood culture in the first and second weeks and by stool culture later on.

The treatment of enteric fever includes bed rest, good hydration, soft diet and antibiotics. It is advisable to start ciprofloxacin 500 mg 12 h orally or if the patient cannot tolerate orally, 400 mg i.v. twice daily. It will take 3 - 5 days for the temperature to settle down and the antibiotic has to be continued for a total of 10 days or for 7 days after the temperature touches normal. If after 3 days of starting ciprofloxacin the general condition is deteriorating or other complications develop it is better to add i.v. ceftriaxone 4 g for 3 days and the case may be referred to a higher centre.

1.3 ACUTE ANAPHYLACTIC REACTIONS

This acute medical emergency can be precipitated by oral or parenteral administration of drugs, or due to inoculation of toxins.

Emergency management includes i.m. injection of 1 mL 1/1000 solution of adrenaline, along with 100 mg i.v. hydrocortisone and i.v. fluids. An i.m. injection of antihistamine (25 mg of chlorpheniramine maleate) may also be given. Proper airways should be maintained and nasal oxygen to be started. Adrenaline and hydrocortisone may be repeated as per the clinical status.

1.4 PREVENTION AND TREATMENT OF PENICILLIN REACTIONS

Prevention of penicillin reactions at the patient level

1. Always have an emergency kit for treatment of allergic reactions readily available
2. Always enquire past history of the patient, previous contact with penicillin, previous penicillin reaction, and allergic diathesis. In infants less than 3 months old, enquire about penicillin allergy in the mother.
3. No penicillin treatment should be given to patients with a previous history of reaction. Indications for administration of penicillin should be restricted in patients with an allergic diathesis. If possible, refer patients with suspected penicillin allergy (preferably within 3 months of the allergic reaction) to a specialist trained in modern immunological techniques, skin testing with penicillin and penicillin derivatives.
4. No penicillin should be employed for external treatment or on mucous membranes, particularly on macerated or eczematized skin, especially if likely to cause sensitization. Cross-sensitivity to the semi-synthetic penicillin is common and there may be harm even for related drugs like cephalosporins at times.
5. Ensure thorough washing and adequate sterilisation of all-purpose syringes that have been used in penicillin treatment when using them to inject other drugs. If possible, use disposable syringes and needles.
6. Observe the patient for at least 30 minutes before discharging him/her from OP.

Treatment of Penicillin reactions

Emergency kit should contain the following items:

1. 1:1000 solution of adrenaline hydrochloride (epinephrine) ready to use;
2. Two 2 mL syringes and hypodermic needles (disposable-type syringes and needles are preferable); and also, if possible;
3. Portable oxygen
4. Hydrocortisone preparation suitable for intravenous injections;
5. Aminophylline, upto 0.5 g for i.v. injection;
6. Antihistamine-chlorpheniramine maleate i.v.
7. i.v. infusion - dextrose saline.
8. Dopamine.

Procedure:

The following procedure should be carried out as quickly as possible:

1. On appearance of signs of reaction immediately make the patient lie down, head down and feet up
2. Inject 0.01 mL/kg adrenaline 1/1000 s.c in the upper arm. If cardiac arrest has occurred use 1/10000 adrenaline 0.1 mL/kg i.v. or via endotracheal tube
3. If immediate response is not obtained, repeat the adrenaline treatment or give an injection of 25mg-100 mg hydrocortisone intravenously.
4. Establish an i.v. line and infuse normal saline if necessary with dopamine 5-10mcg/kg/min.

5. In angioneurotic oedema, urticaria, or conjunctivitis, give anti-histamines.
6. Where there is coughing, dyspnoea, respiratory distress, or substernal discomfort, a slow i.v. injection of aminophylline should be set up. Artificial respiration may be necessary.

2. NUTRITIONAL DISORDERS

1. Nutritional disorders occur commonly in combination, therefore overall nutritional improvement is essential.
2. As far as possible use natural foods which are acceptable and cost effective. For example, sprouted legumes, cereals, unpolished rice, etc
3. Use prepared concentrated foods only sparingly on account of their high cost and unacceptability.
4. When a specific nutritional disorder is encountered the steps to follow are:
 - a. Correction of overall dietary deficiency.
 - b. Medicinal administration of the missing factor.
5. Take care to continue medication for 3 - 6 months after correction of clinical condition in order to build up the stores and thereby prevent relapse.

3. TOXICOLOGY AND ENVENOMATION

3.1 TOXICOLOGY

The common poisons used for suicidal attempt found in Kerala include organophosphorus insecticides, carbamate insecticides, formic acid, plant products such as cerebra odollum, nerium oleandis, zinc phosphide, barbiturates, diazepam, other drugs acting on the CNS, paracetamol and others. Accidental poisoning is often due to organophosphorus insecticides or drugs used by psychiatric patients. Despite this general statement it should be remembered that any type of poison may be involved and the physician should have an open mind.

3.1.1 General management of the poisoned patient

Acute poisoning is a dire emergency. Suicidal poisoning is most common and next in frequency is accidental poisoning.

Evaluation of the poisoned patient

History:

Ascertain the nature, quantity of the poison and the vehicle in which the same was consumed and the time elapsed before patient reaches the hospital. If possible the specimen of the poison left over should be procured for confirmation

If the patient is shocked or unconscious :

1. Start an i.v. line with normal saline through a large bore needle

Guidelines for Clinical Management at the Peripheral Hospitals (18G) or cannula through which fluids and drugs can be administered rapidly.

2. Simultaneously maintain the airway by clearing the mouth and throat of foreign materials, dentures or vomitous and keep the patient with head lowered and neck held in extension. If the patient is unconscious, an airway is inserted.

Some of the salient features of the commonly ingested poisons

Finding	Common cause
1. Aspiration	Organophosphates, kerosene, solvents used for paints, CNS depressants.
2. Behavioural disturbances	Anticholinergics, hallucinogens, CNS stimulants.
3. Bradycardia	Digoxin, beta blockers, organo - phosphates, calcium channel blockers, cerebra odollum, nerium oleandis.
4. Cardiac dysrhythmia	CNS stimulants, theophylline, cardiovascular drugs, cerebra odollum, nerium oleandis.
5. Coma	Barbiturates, diazepam, antidepressants, anticholinergics, ethanol, phenothiazines.
6. Hallucinations	Antihistamines, CNS stimulants, hallucinogens.
7. Hepatic failure	Paracetamol, carbon tetrachloride, INH, mushroom.
8. Hyperpnea	CNS stimulant, CO, salicylate, methanol.
9. Hyperthermia	Phenothiazine, CNS stimulant, anticholenergics.
10. Hypothermia	CNS depressants, alcohol.
11. Intestinal ileus	Narcotic analgesics, anticholenergic, antidepressant.
12. Metabolic acidosis	Alcohol, formic acid, salicylate, other corrosive acids.
13. Nystagmus	Anti convulsants, CNS depressants.
14. Pulmonary oedema	Organophosphates, salicylates.
15. Seizures	Organophosphates, theophylline.
16. Tachycardia	CNS stimulants, anticholinergics, theophylline.

Laboratory tests

1. Qualitative and quantitative analysis are available for a number of poisons and are useful in confirming that a particular drug has been ingested and are of value in screening for unknown drugs. Facility for emergency determination of toxic substance is available at the College of Pharmaceutical Sciences, Medical college, Thiruvananthapuram round the clock, the specimen has to be sent by the physician with clinical details
2. Additional tests that may be of use include arterial blood gas analysis, chest radiograph, and ECG.

Treatment:

Emergency Management of poisoned patient includes

- A. *Decontamination of the poison* which limits the absorption and minimises the extent of toxicity: Clean up the body, remove all contaminated clothing and remove as much of the toxic agent from the oral cavity, pharynx and skin.
- B. *Supportive care* which limits the effects of serious complications of poisoning on the organ systems at risk.
- C. *Definitive care* which limits the severity or duration of toxicity through the use of antidotes and by enhanced elimination of the toxin by forced alkaline diuresis and haemodialysis procedures.

Note :All doctors who see the patients first should undertake the first aid measures, i.e.

1. *Removal of unabsorbed poison from the surface.*
2. *Induction of vomiting.*
3. *Cardio respiratory support.*
4. *Early administration of antidote before referring the patient to a higher centre.*

DECONTAMINATION

The vast majority of serious poisonings are due to ingestion of toxic substances and gastrointestinal decontamination should be done without delay.

1. Syrup of ipecac

- Dose 15 - 30 mL in adults and children above 5 years.
- Stimulates medullary vomiting centre.
- 90 % of patients vomit within 30 minutes.
- S/E : seizures, cardiac toxicity.

In a fully conscious patient tickling the throat induces vomiting. Repetition of vomiting 2-3 times after drinking 300-500 mL of water helps to eliminate the toxic material.

2. Gastric lavage.

- Using large bore (36 - 40 F) orogastric tube.
- Indicated in comatose patients as well as alert patients.
- Patients in Trendelenburg position and left lateral position.
- Decrease risk of aspiration by using cuffed endotracheal tube if available.
- After contents of the stomach are aspirated, aliquots of water at room temperature (50 - 250 mL) should be administered and aspirated until the return is clear.
- Contraindicated in patients who have ingested corrosives or petroleum distillate hydrocarbons.

3. Activated charcoal.

- This acts by adsorbing molecules of chemicals on its surface, thereby inhibiting their absorption
- Dose is 1 g/kg suspended in water and introduced through the orogastric tube.
- 2 or 3 doses of charcoal given at 4 hourly intervals may be of more use than a single administration.

Drugs adsorbed by charcoal

1. Amphetamine
2. Chlorpheniramine
3. Phenytoin
4. Aspirin
5. Cyclic antidepressants
6. Chlorpromazine
7. Quinine

Drugs not adsorbed by charcoal

1. Ferrous sulphate
2. Malathion.
3. Acids
4. Alkalis
5. Alcohol.
6. Lithium.

For better efficacy charcoal should be given before and after gastric lavage.

4. Cathartics (purgatives)

- Include sorbitol, magnesium sulphate, magnesium citrate
- Speed up gastrointestinal motility, thereby shortening the absorption time.

Unabsorbed toxin from the colon can be removed by a large enema (soap and water) or colonic wash out using flatus tube. Samples of materials obtained by vomiting, gastric lavage and colonic wash out should be procured for chemical analysis if a definitive clue regarding poisons has not been obtained.

SUPPORTIVE CARE is directed towards the prevention or limitation of respiratory, cardiovascular and neurological complications.

1. Management of respiratory complications.

Maintain the airway appropriately. Ventilatory support may be needed

in selected cases. If bronchospasm is present use salbutamol nebulisation or an i.v. injection of aminophylline 250 mg diluted in 10% glucose slowly. Non cardiogenic pulmonary oedema may be seen early, requiring treatment with high flow oxygen, positive pressure ventilation and PEEP. Aspiration in to the respiratory tract should be prevented. If it has occurred, try conservative measures such as head low position, gentle tapping on the chest and suction of the tracheo bronchial tree.

2. Management of cardiovascular complications.

Tachyarrhythmias usually requires only monitoring, but may need anti-arrhythmic drugs. Brady arrhythmias are best treated with atropine, but may require temporary transvenous pacing. Hypotension usually reflects decreased peripheral vascular resistance and should be treated with fluid administration, only rarely are vasopressors like dopamine required. Hypertension, which is complicated by pulmonary oedema, cardiac ischemia or encephalopathy should be controlled by direct arterial vasodilators like nitroglycerine or nitroprusside.

3. Management of neurological complications

Coma and altered level of consciousness require special care for maintenance of fluid and electrolyte levels. Seizures can be safely controlled with short acting benzodiazepines (diazepam 5 - 20 mg i.v.) or phenobarbitone (20 mg/kg i.v. at 50 - 100 mg/min). If phenytoin is given, electrocardiogram should be monitored. Behavioural abnormalities including combativeness and agitation are better controlled by physical restraints rather than chemical restraints. Diazepam enables rapid control of unmanageable patients while haloperidol is very effective for long term control.

4. Antidotes :

Next to the general emergency measures, antidotes form the mainstay of successful management of poisonings as early as possible and during the course of treatment blood and urine samples should be sent for drug level monitoring.

DEFINITIVE CARE

1. Specific antidotes

Poison	Antidote	Adult Dosage	Comment
1. Paracetamol	N-acetylcysteine	Initial dose 140 mg/kg orally, then 70 mg/kg 4h	Most effective if given within 16h
2. Atropine	Physostigmine	Initial dose 0.5-2 mg i.v.	Can produce convulsions
3. Carbon monoxide poisoning	Oxygen	100% by face mask or hyperbaric oxygen if available.	Early treatment is successful

Guidelines for Clinical Management at the Peripheral Hospitals

4. Cyanide	Amyl nitrite, sodium nitrite sodium thiosulphate over 5 min, then 50 mL 25% sodium thiosulphate over 10 min	Amyl nitrite inhalation every 2-3 min, then 10 mL of 3% sodium nitrite i.v.	This helps to remove the poison load but action is slow.
5. Iron salts eg. ferrous sulphate	Desferrioxamine	Hypotensive patients 10 mg/ kg/h for 4 h i.v., then 5 mg/ kg/h for 8 h, then 2-5 mg/kg/h. Normotensive patient 40 mg/kg i.m.	
6. Lead salts eg. lead acetate	Calcium disodium edetate	200 mg/mL in ampoule of 5 mL to be diluted in 5% glucose infused i.v. Total dose of 50-75 mg/kg/day in two divided doses, upto 5 days.	
7. Mercury Arsenic, Gold	BAL (dimercaprol)	5 mg/kg deep i.m.	
8. Methyl alcohol	Ethyl alcohol and dialysis	Correction of metabolic acidosis by sodium bicarbonate i.v. Loading dose 0.6-0.7 g/kg. To maintain blood level of 100 mg%	Early management may be successful
9. Nitrites	Methylene blue solution i.v.	0.2 mg/kg of 1% transfusion.	May need exchange
10. Opiates	Naloxone	0.4-0.8 mg iv in adults	
11. Organophosphates	Atropine	2 mg iv initially, maintenance -upto 5 mg every 15 min.	Administration has to be in continuous i.v. drip to maintain pupil size normal. Very large doses of 250-750 ampoules may be required for saving serious cases
	Pralidoxime	initial dose 1 g i.v., to be repeated	
12. Carbamates	Atropine	2-3 mg parenterally and repeat until signs of atropine intoxication appears	

2. Increasing the Drug Excretion

a. Forced alkaline diuresis

- ♦ Especially useful in phenobarbitone and salicylate over dosages.
- ♦ Close monitoring of fluid and electrolytes and pH are required for ideal results.
- ♦ Adequate amounts of sodium bicarbonate (1 - 2 mg/kg/h i.v.infusion) needed to maintain urine pH between 7.5 - 8.5.

C/I: Congestive cardiac failure, renal failure, cerebral oedema

b. Dialysis and haemoperfusion

Dialysis is most effective with drugs of low molecular weights, small volume distribution and low protein binding.

Drugs effectively eliminated by haemodialysis include:

Barbiturates	Lithium salts
Bromides	Methanol
Chloral hydrate	Procainamide
Ethanol	Salicylates
Ethylene glycol	Theophylline
Isopropyl alcohol	

Haemoperfusion is more effective than dialysis in removing drugs with high molecular weight, lipid solubility and protein binding. Examples include

Chloramphenicol	Procainamide
Disopyramide	Theophylline
Hypnotic sedatives	Phenytoin

Peritoneal dialysis and exchange transfusion are less effective but may be used when other procedures are not available, are contraindicated or are technically difficult. (eg. in infants).

c. Activated charcoal

This is given repeatedly in a dose of 1 g/kg bw every 2 - 4 h. Useful in

Carbamazepine	Digoxin	Salicylates
Dapsone	Phenobarbitone	Sodium valproate
Diazepam	Phenytoin	Theophylline

Once the emergency is over these patients should be observed for long term complications such as pneumonia, neuropathy, hepatic damage and others. Suicidal patients should have proper psychiatric management to avoid recurrence.

3.2 ENVENOMATION

3.2.1 Snake envenomation

Diagnosis and management of snake envenomation

Clinical features

Fear, toxicity of venom and side effects of treatment contribute to the symptoms and signs in those bitten by snakes.

Bite by Elapidae (cobra and krait mainly)

Local effects include severe pain, mild oedema, faint bite marks or oozing from the wound. Sometimes local reaction may be absent or only minimal. Systemic effects are dominated by neuromuscular symptoms. Paralysis is first noticed as ptosis and external ophthalmoplegia followed by involvement of face, palate, jaws, tongue, vocal cords, muscles of deglutition and neck muscles. Respiratory muscle paralysis can follow.

Bite by viperidae (vipers)

This produces severe local effects with more prominent bite marks, intense pain, swelling, haemorrhagic oedema and oozing from bite mark. Vomiting is one of the early symptoms of systemic envenomation. Hemostatic abnormalities are characterized by persistent bleeding manifestation. Direct myocardial involvement is suggested by abnormal ECG and arrhythmias and refractory hypotension. Renal failure is the leading cause of death and clinically it manifests with acute oliguric renal failure.

Laboratory diagnosis

The one that helps to determine and maintain antivenom therapy is the clotting time which prolongs above 10 minutes. Thrombocytopenia is common in viper bite. Fibrinogen is often reduced, APPT and PT are prolonged. Oliguria, proteinuria, haematuria and red blood cell casts may be seen in those with renal involvement. ECG abnormalities may be seen.

First Aid

If the bite occurs in the presence of a witness undertake the following:

- Site of bite should be washed with soap and water three times, allowing some blood to ooze freely
- Bitten limb should be immobilised with a splint or sling.
- Patient should be reassured and moved to the nearest hospital as soon as possible.
- Local incisions and suction are of limited value. At times they may be harmful.
- A tourniquet or preferably compressive crepe bandage should be applied firmly proximal to the bitten site in order to occlude the lymphatic circulation mainly.
- The patient should be encouraged to take plenty of oral fluids.

Hospital Management

Essentials of hospital treatment consist of rapid assessment of the bite and its complications and early administration of antivenom in cases with evidence of bite by poisonous snakes. Even patients with mild or inapparent symptoms, should be observed for upto 24 hours, since delayed envenomation is not rare.

Indications for Anti-snake venom (ASV)

This is prepared by the Haffkine Institute Bombay, and Serum Institute of India, Pune. The available preparation is polyvalent ie. active against cobra, krait and viper.

(Storage: Antivenom should be stored at 2-8°C, it should not be allowed to freeze and the shelf life is 4 years after manufacture).

Indications (evidence of systemic envenomation)

- ♦ neurotoxic signs.
- ♦ recurrent vomiting.
- ♦ haemostatic abnormalities
- ♦ cardio vascular signs.
- ♦ impaired consciousness.
- ♦ general rhabdomyolysis.
- ♦ severe local reaction even in the absence of systemic signs.

ASV should be given as early as possible for the best results and the dose may have to be repeated often, depending on the clinical status.

Note: Before going to the full dose of ASV a sensitivity test should be done as follows: 0.1 mL i.d. test, if no reaction occurs 0.5 mL diluted in saline given i.v. to test for reaction and if there is no reaction full dose of ASV is given. Hypersensitivity is uncommon and can be managed with i.v. hydrocortisone.

Dose of antsnake venom

When only local reaction is present

Give 3 - 6 vials of ASV after test dose as an infusion in 20 min and observe for other signs of envenomation.

When systemic envenomation is present

10 vials of ASV as an infusion in 20 - 30 min and simultaneously start 6 vials of ASV in 5% glucose as drip to be run in 4 - 6 h.

When to repeat ASV

ASV is to be given if several signs of envenomation persists after 1 - 2 h or if the clotting time is not restored within 6 h. Clotting time is to be repeated every 4 - 6 h and ASV administration repeated if necessary. *Better late than never is to be the policy with ASV. It is atleast partially useful in patients with signs of systemic envenomation who come even a few days after the bite.*

In the vast majority, attention to the local site is also necessary. This should include cleaning, wound toilet, absorbent dressings and partial immobilisation of the limb. Antibiotics active against multiple infections has to be started. Ampicillin (0.5 g i.v. / i.m. 6 h) or cloxacillin (250 - 500 mg 6 h) are reasonably good choices. Anaerobic infection demands the use of i.v. metronidazole 500 mg t.d.s. Tetanus prophylaxis has to be given to nonimmunized persons.

Special problems in viper bites

Prevention of APF in viper bite is by prompt administration of ASV plus maintaining fluid volume. Coagulation disturbances is to be treated

with fresh blood or blood components. Volume replenishment should be stressed as patients can have severe hypovolemia due to several factors. Normal saline, plasma expanders and blood should be used judiciously as indicated. If patient is oliguric, conservative measures for treating ARF should be instituted. Antivenom has to be stocked in all the primary health centres at all times. Dialysis is indicated once acute renal failure is established. As snake venom is not dialysable there is no role for prophylactic dialysis.

Special problems in elapidae bites

These may cause acute myasthenic crisis due to neuromuscular blocking action of the toxin. They may present as acute respiratory paralysis, not readily relived by ASV. Neostigmine given in a dose of 0.5 mg i.v. repeated at short intervals is dramatically effective and life saving. If the respiratory failure is not relieved promptly, ventilatory support is required and the patient has to be rushed to a proper centre.

3.2.2 Bee and wasp stings

These are common. Most of the cases are mild and they clear up spontaneously. Multiple stings and especially on the face and head may give rise to severe local reactions, angioneurotic oedema, respiratory obstruction and death. Persons who are sensitised by previous exposure are at higher risk of angio neurotic oedema of the face, anaphylaxis and death.

- Stingers embedded in skin should be scraped or brushed off with a nail or finger nail but not removed with forceps, which may squeeze more **venoms out of the venom sac.**
- **The site should be cleansed with soap and water**
- Ice packs applied locally slow the spread of the venom.
- Elevation of affected site. Administration of analgesics such as paracetamol 600mg orally and antihistamines such as chlorpheniramine (4 mg) and diphenhydramine (25 mg) provide symptomatic relief. If the local reaction is moderate or severe, oral prednisolone (20 mg) or injection betamethasone or dexamethasone (4 mg) should be given.
- Anaphylactic shock and respiratory obstruction demand emergency management. Emergency management in the presence of anaphylactic shock is to give 1 mL of adrenaline (epinephrine) 1 in 1000 solution i.m., repeated if necessary. Upper airway obstruction is managed by emergency tracheostomy or tracheal intubation. In a dire emergency with only poor medical facilities, the airway can be temporarily established by sticking in 3 - 4 wide bore hypodermic needles through the cricothyroid membrane. The patient should be immediately transported to the nearest hospital where better care is available. Hydrocortisone 100 mg or betamethasone 4 mg or dexamethasone 4 mg should be pushed in by i.v. route, followed by 25 -50 mL of 25% glucose. If the conditions does not clear up promptly an i.v. line should be established for further medication

- ♦ Since delayed complications such as coagulopathy and renal failure may occur these should be watched for. Persons allergic to these stings should be warned to avoid further exposure.

4. PAEDIATRICS

4.1 DIARRHOEA AND DEHYDRATION

Common signs of dehydration are increased thirst, restlessness, dry tongue and decreased skin turgor. In severe dehydration there will be obtundation, floppy limbs, low volume pulse and oliguria.

In mild diarrhoea child has none of the signs described above and the main goal of treatment is to replace ongoing losses using homemade fluids like salted kanji water or ORAL REHYDRATION SOLUTION (ORS).

Dose: 1 packet of ORS dissolved in 1 L (5 glass) of potable water (boiled and cooled).

After each motion give ORS

50mL (1/4 glass) for infants <6 months,

1/2 glass for children upto 2 years and

1 glass for older children.

Use cup and spoon to give ORS. Breast feeding should be continued in small frequent feeds.

In moderate dehydration: ORS/IV fluids will be required. About 100 mL/kg ORS is given in 4 h. Breast feeding to be continued. Offer plain boiled water in between ORS in those who are not breast fed. Home made fluids like salted rice water, coconut water or buttermilk can be used. IV fluids are used in similar lines for the treatment of severe dehydration (see below) except the initial emergency phase can be omitted.

In Severe Dehydration: always use i.v. fluids. Shock, acidosis and marked oliguria by themselves are indicative of severe dehydration. Ringer lactate or Normal saline is used initially

Dose: 30mL/kg in first 1h followed by 70mL/kg over next 5 h.
(100mL/kg in 6 h).

Dextrose saline may be used instead to prevent hypoglycaemia.

For older children 100mL/kg should be given in 4 h. Add KCL 20mEq/L as soon as child passes urine. In cholera much more fluid will be required and constant monitoring of hydration is essential. ORS and feeding can be started at the end of 6h as the signs of dehydration disappears by this time. The i.v. fluid can then be changed to maintenance fluid if required eg. isolyte P. Holliday and Segar Formula is generally used to calculate maintenance requirement as given below.

Dose: First 10 kg - 100 mL/kg/24 h.

10-20 kg - 1000 + 50 mL/additional kg over 10 kg.

Guidelines for Clinical Management at the Peripheral Hospitals

Above 20 kg - 1500 + 20 mL / kg for additional kg over 20 kg

Ongoing losses also should be replaced.

Use 7.5% soda bicarb. 2 mL / kg diluted with equal amount of distilled water or 5% dextrose i.v. slowly in severe acidosis.

Diarrhoea and Dehydration

eg. 1 year old weighing 10 kg

	Symptoms & signs	Fluid deficit eg. 2 yr old Wt. 12 kg	Fluid replacement as ORS
Mild	None	500 mL	½ glass = 100mL after each stool
Moderate	Restless Thirst increased Skin turgor -- Dry mouth.	500 - 1000mL	In first 4 h, 600-800mL (3 to 4 glasses of ORS)
Severe	Lethargic Floppy Cold extremities rapid thready pulse hr 70mL/kg fluid	>1000 mL	IV Fluid required 1 st 6 hour 100mL/kg Ringer lactate / N saline) 1 st hr 30 mL/kg Next 5 thereafter maintenance if required.

Antidiarrhoeals are contra indicated. Antibiotics are not necessary except in invasive diarrhoea characterised by blood in stools.

Dose: Nalidixic acid 55mg/kg in divided dose for 5 days is effective in cholera.

Dose: Tetracycline 50mg/kg in divided dose for 3 days is recommended as the first line drug.

4.2 ACUTE LOWER RESPIRATORY TRACT INFECTIONS (LRTI)

Acute lower respiratory tract infections in children may manifest mainly in 3 ways.

- 1) As upper airway obstruction eg. croup
- 2) Obstructive airway disease eg. acute bronchiolitis
- 3) Pneumonia
- 4) Wheezing associated with viral LRTI is common in children and most tend to disappear later.

Croup-characterised by brassy cough, hoarseness, inspiratory stridor and dyspnoea. Some may have associated bronchospasm and called acute laryngo tracheo bronchitis. Most of these are viral infections. Serious bacterial infections like acute epiglottitis caused by *Haemophilus influenza*, laryngeal diphtheria and retropharyngeal abscess may present in a similar way.

Examination of throat should be undertaken carefully as there is a risk of sudden laryngospasm and respiratory arrest. These children are better admitted to hospital for observation.

Treatment : Steam inhalation is helpful. Corticosteroids i.v. or by nebulization (budesonide respirator solution) is useful . Some may benefit from nebulized salbutamol especially when accompanied by bronchospasm. Antibiotics are given when bacterial infection is suspected. Sedation should be avoided.

Acute bronchiolitis -mainly affects infants 3 to 6 months of age. Commonest organism is respiratory syncytial virus. It often occurs in epidemics soon after monsoon season. There is mild fever, running nose, cough and signs of emphysema due to obstruction of bronchioles by inflammatory exudate. Chest x-ray is normal or may show hyperinflation and patchy areas of atelectasis.

Most cases needs only continued breast feeding and paracetamol for fever. Cough mixtures and nasal drops should not be used. Nebulized salbutamol is useful in some infants. Steroids are also used in severe cases, although its usefulness is controversial. Antibiotics are required in severe cases or when bacterial infection is suspected.

Majority of pneumonia in developing countries are bacterial. Pneumococci, Haemophilus influenzae and Staphylococcus aureus are common pathogens. Pneumonia is recognised by fast breathing. The severity of pneumonia is recognised by chest indrawing. In very severe disease there are some danger signs as shown in the table below. These signs have been found to be as specific and more sensitive in children than auscultation of chest.

Fast breathing is present where the respiratory rate is

- ♦ 60 or more in a child less than 2 months;
- ♦ 50 or more in a child 2 to 12 months;
- ♦ 40 or more in a child 12 months to 5 years;

Danger signs are

- ♦ Refusal or decreased acceptance of feeds
- ♦ Excessive drowsiness and difficulty to wake
- ♦ Respiratory grunting
- ♦ Wheezing
- ♦ Stridor
- ♦ Cyanosis
- ♦ Convulsion
- ♦ Severe Malnutrition

In a child with cough or difficulty in breathing

- ♦ Fast breathing indicates Pneumonia
- ♦ Fast breathing and chest indrawing indicates severe Pneumonia
- ♦ Presence of danger signs indicate very severe disease

Cases of severe pneumonia and very severe disease should be admitted

Guidelines for Clinical Management at the Peripheral Hospitals

to hospital for investigation and treatment. Pneumonia accompanied by fast breathing alone can be managed at home. Oral cotrimoxazole is effective for these children in a dose of 6-8 mg/kg/day in 2 divided doses.

Severe pneumonia is treated with benzyl penicillin 200000units/kg/day or Ampicillin 200mg/kg/day or chloramphenicol 100 mg/kg/day all divided into 6 hourly doses depending on severity. Oxygen, IV fluids and other supportive measures should be given when necessary.

Cases of very severe disease need further investigation to detect any associated disease like septicaemia or Meningitis. Treatment of staphylococcal pneumonia is described elsewhere.

4.3 ACUTE SEVERE ASTHMA (in children)

In acute severe asthma early detection of severity of attack and prompt treatment is essential to prevent mortality.

Signs indicative of acute severe asthma:

1. too breathless to feed or talk,
2. respiratory rate over 40/min together with use of accessory muscles,
3. chest retraction,
4. tachycardia over 140/min
5. fatigue and exhaustion,
6. reduced level of consciousness,
7. silent chest on auscultation, cyanosis,
8. sudden onset of bradycardia and poor respiratory effort are all indicative of life threatening asthma. Inhaled beta2 agonist

is the drug of choice.

- a) Beta2 agonists. salbutamol/ terbutaline, preferably using a Nebuliser. Dilute 0.5 mL (2.5mg) salbutamol respirator solution with 4 mL normal saline and place it in the nebulization chamber. Using pressurised air or oxygen the solution can be nebulized into fine particles which the child inhales using a mask or mouth piece. Repeat nebulisation 4-6 hrly or earlier as needed.
- b) In small children the dose is calculated as 150 mcg/kg/dose of salbutamol respirator solution diluted with 10 times volume of normal saline and then nebulised.
- c) If a nebulizer is not available a metered dose inhaler can be used in a dose of 2 puffs of salbutamol every 4 to 6 h or earlier. Volumetric spacer or a plastic cup can be used for administering the drug in small children.
- d) Parenteral dose is 5mcg/kg of terbutaline/dose every 6th hrly s.c or it can be given as a bolus dose diluted followed by an i.v. infusion at a rate of 0.1 mcg/kg/minute of terbutaline, increasing 0.1 mcg/kg every 15 minutes to a maximum of 4 mcg/kg/minute.
- e) Anticholinergic drug like Ipratropium bromide 0.5ml-1ml (125-250mcg) can be added to salbutamol nebulizer solution and then nebulized every 4-6 hrly in severe cases.

- f) Aminophylline. bolus dose of 6 mg/kg/diluted i.v. very slowly followed by an infusion of 0.7-0.9 mg/kg/h. Give only 3 mg/kg as bolus if child is already on theophylline or omit the bolus dose.
- g) Hydrocortisone. 5 to 10 mg/kg/dose. Repeat 4 to 6 hrly or earlier in severe cases.
- h) Oxygen inhalation and other treatment modes like antibiotics, alkali therapy, and IV fluid if indicated. No sedation, but monitor carefully. Very few cases may need artificial ventilation to save life.

4.4 STAPHYLOCOCCAL PNEUMONIA

Staph pneumonia is usually seen in infants and young children and carries a high mortality unless early and adequate treatment is given. The pneumonia is accompanied by the appearance of pneumatoceles in x-ray and rapid progression to produce empyema and pyopneumothorax.

Treatment :

Cloxacillin

Dose: 50 - 100 mg/kg/24 h i.v. initially every 6 h x 4 weeks + gentamicin/ amikacin x 10-14 days.

First generation cephalosporins are effective but watch renal function if used in conjunction with aminoglycosides.

Amoxycillin + clavulanic acid /sulbactam or chloramphenicol can be used and are effective.

Intercostal drain with a large bore tube and under water seal is required for the treatment of empyema.

4.5 PYOGENIC MENINGITIS

Neonatal meningitis carries high mortality and morbidity and treatment should not be undertaken lightly unless adequate facilities are available. Since early institution of specific therapy is the single most important prognostic factor for recovery, it is advisable to give a dose of ceftriaxone 100 mg/kg/kg i.m. or i.v. if there is likely to be a delay in referring the patient to the higher centre.

Suggested Schedule

New born meningitis

1. Ampicillin 200-300 mg/kg/24 hrs in divided doses 6 h + Gentamicin 5-7.5 mg/kg/24 hrs in divided doses 8-12 h.
Better choice will be
2. Cefotaxime 200 mg/kg/24 hrs in divided doses 6 h + Amikacin 15 mg/kg/24 hrs divided dose every 12 h

Meningitis beyond infancy

1 Crystalline penicillin (penicillin G) 400000 units/kg/24 hrs divided dose, 4 h+ Chloramphenicol 100 mg/kg/24 hrs in divided dose 6 h or Ceftriaxone 100 mg/kg/24 hrs in divided dose every 12 h is considered the drug of choice.

Guidelines for Clinical Management at the Peripheral Hospitals

A combination of Crystalline Penicillin + Ceftriaxone is recommended. Generally treatment is continued for 10-14 days.

Dexamethasone 0.15 mg/kg/dose every 6 h for 2-4 days is beneficial to decrease the complication of nerve deafness, in H. Influenza meningitis if started before antibiotics.

4.6 PRIMARY TUBERCULOSIS (in children)

Primary Tuberculosis. Treatment of choice 2HRZ/4HR. First 2 months: INH 5-10 mg/kg/day + Rifampicin 11 mg/kg/day + Pyrazinamide 30 mg/kg/day. After 2 months: INH 5 mg/kg + Rifampicin 11 mg/kg once daily for 4 months.

In disseminated tuberculosis the treatment recommended is 2HRZE/7HR (2 months INH, rifampicin, pyrazinamide + ethambutol followed by 7 months INH and rifampicin). A fourth drug ethambutol 20 mg/kg is added in the first 2 months of therapy. Streptomycin 20-30 mg/kg/day can be used instead of Ethambutol but rarely used nowadays.

In Tuberculous meningitis and neurotuberculosis in addition to the above drugs use steroids in the initial phase. Total duration of treatment is 12 months. Recommended schedule is 2HRZE/7HRE or 10 HRE. If no resolution of symptoms, liver function should be monitored and stop hepatotoxic drugs if transaminase levels are 3-4 times above normal.

4.7 RESUSCITATION OF NEWBORN

- ♦ Evaluate the neonate at birth for adequacy of respiration, heart rate and colour.
- ♦ Most newborn babies cry immediately at birth. Dry the baby in a clean warm towel.
- ♦ If baby has not cried within 15-20 seconds after birth or if baby is apnoeic or gasping, place the baby on a flat resuscitation table under a warmer with head slightly extended by 30 degrees.
- ♦ Clean the airway by oropharyngeal suction, mouth first, then nose.
- ♦ Provide tactile stimulus by flicking the soles.
- ♦ Do not slap the baby or hang him upside down.
- ♦ If baby is still gasping/apnoeic immediately initiate assisted ventilation with a bag and mask using oxygen at 2-4 L/min. Use of oxygen reservoir will enable 100% oxygen administration.
- ♦ Count heart rate with a stethoscope for 6 seconds and multiply by 10 to get heart rate in 1 minute.
- ♦ If heart rate is less than 60 or fails to rise above 80 after 30 seconds of assisted ventilation, then initiate external cardiac massage by chest compression 120 times a minute. For every 2 chest compression one ventilatory breath is given.
- ♦ If no response to bag and mask ventilation and chest compression

then endotracheal intubation and positive pressure ventilation is given using oxygen.

- ♦ Endotracheal intubation is indicated if meconium aspiration or diaphragmatic hernia is suspected. Do not use bag and mask ventilation in these circumstances.
- ♦ If mother had received a narcotic within 4 hours prior to delivery then give naloxone 5-10 mg/kg or nalorphine 0.1 mg/kg i.v or i.m.
- ♦ Hypoglycaemia should be anticipated and corrected. Give 25% glucose 1 mL/kg over 4 min initially and then continue with 10% dextrose infusion 60-90 mL/kg/day.
- ♦ If heart rate remains less than 80/min despite adequate resuscitation, give 1/10000 adrenaline 0.1 mL/kg i.v./via endotracheal tube or rarely intracardiac.
- ♦ If the baby is in shock with poor peripheral pulse and circulation expand volume with N.saline / Ringer lactate or plasma 10 mL/kg.
- ♦ Dopamine infusion 2-20 mcg/kg/min may be used if shock does not improve.
- ♦ If after 8-10 min of adequate resuscitation baby does not show signs of improvement and acidosis is severe, then NaHCO_3 (7.5%), 2 mL/kg/diluted with equal amount of distilled water is given slowly over 2-3 min.

4.8 POISONING IN CHILDREN

Diagnosis of poisoning in children is easy when history is forthcoming. But it should be suspected in any healthy toddler with acute onset of unexplained symptoms like drowsiness or delirium. Commonest poisoning is due to kerosene oil and iron tablets although a variety of drugs, chemicals, insecticides and vegetable poisons can lead to mild or serious poisoning. Traditional doctors may use powders of mercury and dubious medicines like "Mulleli Thylum and Motta thylum" and these can sometimes cause serious poisoning. Physical examination should focus on vital signs, cardiopulmonary and neurological status. If child is seen soon after ingestion, vomiting should be induced, preferably with syrup of Ipecac 15 mL followed by a drink of 1 glass of water or fruit juice. It can be repeated in 20 minutes if vomiting does not occur. If induction of emesis is not successful gastric lavage should be done carefully using a wide bore tube. 30 -50 mL water or 1/2 N saline is introduced each time and then aspirated until returning fluid is clear. Specific antidote if available should be given immediately -eg. Desferrioxamine for Iron poisoning. Close observation and masterly inactivity is all that is required in most cases. Symptomatic and supportive treatment will be required in some severe cases eg. anticonvulsants, correction of acidosis and fluid-electrolyte balance, oxygen etc. Organ dysfunction should be monitored and prevented and supportive treatment initiated without delay. Renal excretion of poisons like salicylate and phenobarbitone can be hastened by forced alkaline diuresis or dialysis. At

Guidelines for Clinical Management at the Peripheral Hospitals

the time of discharge parents should be advised on prevention of poisoning since most poisoning in children are accidental.

4.8.1 Some Common Poisoning in Children and their Management

No.	Poison	Cli.features	Treatment
1.	Acids	Severe pain, erythema and swelling/ulceration of mouth. Laryngeal oedema-watch for shock, renal failure	No emetic/lavage cold water/milk, i.v. fluid antibiotic \pm steroid surgical consultation
2.	Alkali eg. bleaching powder	pain, swelling, white plaques in the mouth Dysphagia, drooling	No emetics/lavage. Cold water/ milk i.v. fluid, antibiotic, surgical consultation
3.	Aspirin	Vomiting, flushing, tinnitus abd Pain, GI bleed, acidotic breathing seizure, coma. hypoglycaemia, salicylate level $>100\text{mg/dL}$ in severe poisoning	Lavage, emetics Fluid electrolyte therapy. Correct acidosis, Glucose, Vit.K, forced alkaline diuresis. Dialysis
4.	Datura	Tachycardia, fever, dilated, pupil flushing, delirium, urinary retention	emetics or lavage. Paracetamol for fever, physostigmine $0.02\text{-}0.06\text{ mg/kg s.c. Rpt. after } 10\text{ min}$ if needed. Catheterise for retention of urine
5.	Kerosene oil	Vomiting, cough, breathless, smell of kerosene, coma, chest x-ray, mottled appearance	No emetic or lavage. Oxygen, cyanotic, crystalline penicillin in case of aspiration; salbutamol and steroid in case of wheezing
6.	Iron	5 stages <u>step 1.</u> Within hours, vomiting, abd.pain, GI bleed. <u>Step 2.</u> of apparent recovery for few hrs <u>step 3.</u> After 12 h. shock encephalopathy, acidosis <u>Step 4.</u> 2-4 days, hepatic failure <u>Step 5.</u> 2-4 weeks gastric scarring and int. obstruction.	Emetic/lavage, chelation as early as possible. Desferrioxamine i.m. or i.v. Continue till urine is clear. vin rose colour if serum Iron is high.

7. Organophosphorous Sweating, salivation, small pupil, emetics/lavage. clean any
lacrimation bradycardia, skin contaminated.
hypotension, twitching, seizure, symptomatic and
coma, pulmonary oedema, supportive. Atropine
vent-. arrhythmia . 0.05mg/kg i.v. at 5-10 min
Choline esterase activity in interval as needed
RBC/ serum <20% in severe cases. Pralidoxine 25-50mg/kg/
i.v. as a 5% solution after
atropinisation,
haemodialysis may be useful
8. Paracetamol Nausea, vomiting, hypoglycaemia, Emetic/lavage. N. acetyl
hepatic failure usually on 3rd day. cysteine initially oral -
Renal failure, coma. 140mg/kg, then 70mg/kg
every 4 h, 17 such doses.
i.v. 150 mg/kg i.v. diluted
as loading dose. Then
50mg/kg in 5% dextrose
over 4-8 h x 3 doses

5. IMMUNISATION

Immunodeficient subjects do not put up immunological defence by vaccination. Immunisation is the safe and specific preventive measure against infection in immunocompetent hosts .

5.1 Active Immunisation

- Live, attenuated form of infective agent, e.g.: Rubella, measles, mumps, B.C.G., sabins vaccine for poliomyelitis
- Killed or inactivated forms. eg. Typhoid vaccine, Salk vaccine, Cholera vaccine, Pertussis vaccine.
- Extracts of micro-organism or toxoids administered parenterally eg. Diphtheria, tetanus toxoid.

The response associated with initial encounter with vaccine is called primary immunisation. Following subsequent exposure of the immunised host to the same, antibody production occurs much sooner and quicker at short latent period and antibody levels are higher. The vaccine used for revaccination is also called as the booster dose.

5.2 Passive Immunisation

Immunity with immediate protection against certain infective organisms can be obtained by preparations made from the plasma of immune individuals with adequate levels of antibody to the disease for which protection is sought. This passive immunity lasts only for a few weeks, and therefore, passive immunisation has to be repeated for continued protection. Antibodies of human

Guidelines for Clinical Management at the Peripheral Hospitals

origin are usually termed immunoglobulins. The term antiserum is applied to material prepared from animals. Because of serum sickness and other allergic type of reactions that may follow injection of antiserum, they have been replaced wherever possible by the use of immunoglobulins. These reactions may develop after injection of human immunoglobulins. Such reactions are rare, and if at all they occur, they are milder.

5.3 Common side effects to vaccine and their management

Side effects are rare and are usually transient. It may be local or systemic. It is mandatory that every immunisation clinic should have an emergency set up to deal with any severe adverse event. Mild cough and cold are not contraindications to vaccination. Fever and mild local swelling and tenderness are fairly common and should be treated with paracetamol alone for one or two days. Left axillary lymphadenitis may follow BCG vaccination. Small nodes are better left alone. Once fluctuation occurs incision and drainage is the best course of action followed by a course of antibiotic. Large lymph nodes and fluctuating nodes if associated with positive Mantoux test should be treated with INH and rifampicin for 6 months. Mild fever accompanied by a fine rash can occur after measles and MMR (Measles, Mumps, Rubella) vaccination and this tend to disappear in 2 or 3 days. No treatment other than paracetamol for fever is necessary.

Adverse Events following Immunisation (IAP Guide Book on Immunisation)

Sno.	Adverse Event	Vaccine	Symptom	Management
1.	Anaphylaxis	Any vaccine	Within minutes Acute decompensation of circulatory system Hypovolemic shock Altered sensorium Laryngospasm/oedema Acute respiratory distress	Adrenaline Cardiopulmonary resuscitation i.v. volume expanders Oxygen Dopamine/Dobutamine
2	Hypotensive-hyporesponsive episode	DPT	Within 12 hours Acute paleness Transient decreased level or loss of consciousness, decrease or loss of muscle tone	i.v. fluids Dexamethasone Oxygen
3	Incessant Cry	DPT	Within 48 to 72 hours after DPT immunisation Excessive inconsolable crying	Sedation is of little help Feeding advice Avoid DPT for subsequent dose/s

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4.	Toxic shock syndrome	Contamination of measles vaccine by Staph. aureus Septic shock	Within 30 minutes to few hours Mounting fever Vomiting Diarrhoea Supportive therapy	i.v. fluids Antimicrobials Steroids Antipyretics
5.	Lymphadenitis	BCG	Within 2 to 6 months Firm to soft axillary lymphadenitis *HR 9, aspiration if with or without sinus	If firm no treatment If soft and fluctuant 1.5 to 3 cms size need be If sinus present steroid therapy
6.	Bacterial abscess	any vaccine	Within 72 hours fluctuant or firm abscess with or without fever	Antibiotics Antipyretics Drainage (if need be)
7.	Sterile abscess	DPT, DT TT, Typhoid and HB	By 72 hours Minimum inflammation No fever	Drainage if need be
8.	Moderate local reaction	Any vaccine	Non fluctuant swelling/redness approx. 3 cm to 10 cm in size at the injection site	Paracetamol local heat
9.	several local reaction	Any vaccine	non fluctuant swelling/redness 10 cm size or larger at the site of inj.	Paracetamol local heat
10.	Seizure/with fever(rare)	DPT Measles	Always generalised simple or complex	Anticonvulsants Antipyretics i.v. fluids if need be

*HR 9 = INH+Rifampicin for 9 months

Contraindication to immunisations:

1. History of sensitivity or allergy to preservative or any other component used in vaccine.
2. Rubella vaccine is contraindicated in pregnancy.
3. Severe febrile illness.
4. HIV positive subjects can receive measles, mumps, killed polio vaccine, rubella vaccine and those against cholera, diphtheria and

Hepatitis B. HIV positive subjects should not receive O.P.V, B.C.G and yellow fever vaccine.

5. In immunocompromised children live vaccines should not be given. Attenuated vaccines are less immunogenic.
6. Pertussis vaccine is contraindicated in progressive neurological disease, uncontrolled seizures and previous severe reaction to DPT vaccination.

Misconception concerning contraindications:

Prematurity, common cold, intercurrent antimicrobial therapy, breast feeding, non-specific allergy, history of seizures, history of mild adverse reaction to immunisation and static CNS diseases are not contraindications for immunisation.

Vaccine preventable disease in children:

In the developing world each year 3 million infants and children die and another 3 million become seriously handicapped due to six vaccine preventable diseases like diphtheria, pertussis, tetanus, poliomyelitis, measles and tuberculosis.

In India, with improved status of immunisation in recent years, death from vaccine preventable disease has decreased significantly.

5.4 Vaccines Mandatory for all children

National schedule of Immunisation

At birth :B.C.G. vaccine and zero dose oral polio vaccine.

6 weeks 1st dose OPV + DPT

10 weeks 2nd dose OPV +DPT

14 weeks 3rd dose OPV+DPT

Measles vaccine after 9 months of age

18 months -1st booster OPV+DPT

4-5 years -DT only.

At 10 years and 16 years Tetanus toxoid.

(DPT = Diphtheria, pertussis and tetanus; DT = diphtheria and tetanus; MMR = Measles, mumps and rubella; OPV = oral polio vaccine)

(MMR is given at 15 months though not included In national schedule)

Schedule to be followed if unimmunised child presents for the first time after 1 year:

	1-5 yrs	More than 5 years
1st visit	BCG,DPT,OPV	DT, BCG
2nd visit	DPT, OPV	DT
3rd visit	DPT, OPV, Measles	DT
1 yr. Later	DT,OPV	DT

DPT is contraindicated after the age of 5 years. If there is delay in 2nd dose it is not necessary to restart the whole course, the remaining dose need only be given.

Storage of Vaccines and expiry date of vaccines:

Vaccines must be stored at a temperature between 2-8°C and should not be allowed to freeze unless otherwise specified in the individual monograph. Freeze - dried preparations must be stored at a temperature below -20°C or as specified on the label of the preparation. Note the expiry date of the preparation given on the label. At higher temperatures vaccines deteriorate rapidly.

5.4.1 BCG Vaccine (Bacillus Calmette Guerin)

Freeze dried preparation of live attenuated bacteria of a strain derived from Bacillus Calmette and Guerin. Store frozen or refrigerated. Use reconstituted BCG within 4-6 hours. Premature babies should be vaccinated after their birthweight has reached 2kg.

Dose: 0.1 mL i.d. in deltoid region. The individual becomes mantoux positive in 8-14 weeks. A second dose should be given if no scar develops at the injection site. Older children who did not receive BCG earlier should be subjected to Mantoux test and if negative BCG is indicated. The vaccine efficacy is in the range of 70-80% against severe forms of TB like miliary and TB meningitis and only 50% against secondary (adult) forms of tuberculosis.

BCG is available with primary health centres, district hospitals, all the T.B.centres and several other government and non government health institution

Storage: Store in light resistant glass containers at a temperature between 2-8°C. The vaccine should be used immediately after reconstitution.

Tuberculin Test

Tuberculin Purified Protein Derivative

Purified protein derivatives (PPD). (Mantoux Test)

PPD is prepared from the heat treated product after growth and lysis of the appropriate species of mycobacterium. In the Mantoux test, the antigen is 1 unit of tuberculin PPD with Tween 80 in 0.1 mL is given by intradermal injection on the volar aspect of left forearm 10 units/0.1 mL is available commercially. This may give false positive result

P/A: PPD - King Institute. 5 mL (10 unit / 0.1 mL)

Storage : Store in light resistant containers at a temperature between 2-8°C. It should not be allowed to freeze.

5.4.2 Poliomyelitis Vaccine

Live attenuated trivalent vaccine (Sabin vaccine). The vaccine is a suspension of over 1 million particles of poliovirus type 1, 2, and 3. It is supplied with a stabilising agent namely magnesium chloride and is suitable for oral administration. Vaccine is inactivated by high temperatures

C/I : Acute infection, diarrhoea, malignancy, patients getting

Guidelines for Clinical Management at the Peripheral Hospitals
chemotherapy, radiation therapy, immunocompromised patients,
pregnancy.

- S/E: Vaccine associated poliomyelitis occurs about one in five million vaccinated persons.
- Dose: 2 drops given orally in 3 doses at monthly intervals along with Triple antigen. Booster dose is given at 18 months. Pulse polio immunisation is aimed at eradicating poliomyelitis. To achieve this all children below 5 years are given two doses of polio vaccine annually on 2 fixed days. Polio vaccine (oral) Haffkine. 10 mL (20 dose)
- Cost: 2 mL vial x 50 Rs.80.00
- Storage: Store at -20°C or refrigerated $2-8^{\circ}\text{C}$.

5.4.3 Measles Vaccine

Live attenuated measles virus grown in chick embryo fibroblast culture (Schwartz vaccine) or Edmonston-Zagreb strain of measles vaccine propagated in human diploid cells. Freeze dried vaccine. Store frozen or refrigerated and use within 4-6 hrs after reconstitution as subcutaneous injection.

- I: Prophylaxis against measles.
- C/I: Uncontrolled convulsion, Pregnancy, acute infectious disease, active TB, allergy to egg proteins, neomycin and polymyxin, malignancy, impaired immune response.
- P/C: Do not administer intravenously. Vaccine to be delayed for 3 months for those who have received human gammaglobulin or blood transfusion.
- S/E: Mild measles like response with fever, and rashes which come on 1 week after injection. Subacute sclerosing panencephalitis is very rare. This occurs at the rate of 5-10 case per million doses. It appears that measles vaccination to some extent protects the children against SSPE. Severe neurological complications like encephalitis following measles vaccine are extremely rare, and 12-20 times less common than natural measles infection. Vaccine contaminated with *Staph aureus* may cause toxic shock syndrome, which can be rapidly fatal unless treated promptly.
- Dose: 0.5 mL s.c. preferably right upper arm. Rouvax measles vaccine-Serum Institute. 10 dose vial.
- Storage: Store in light resistant containers at a temperature between $2-8^{\circ}\text{C}$ when stored under the prescribed conditions the vaccine may be expected to retain its potency for not less than 24 months from the date of last determination of the virus titre.

5.4.4 Triple Antigen (Diphtheria, Pertussis, Tetanus) DPT Vaccine

Vaccine adsorbed on aluminium phosphate is popularly known as Triple Antigen (DPT) The combination of diphtheria toxoid, tetanus toxoid and whole cell killed pertussis vaccine). While the two toxoids give almost 100% protection,

the protective efficacy of pertussis vaccine is only 70-80%. Acellular pertussis vaccine is used in Western countries as it has less side effects.

- I: Prophylaxis against diphtheria, tetanus, and whooping cough in children under age of 5 years.
 - C/I: DPT should not be given to children above 5 years of age, acute febrile illness, progressive neurological disorders and allergy to pertussis vaccine.
 - P/C: Triple antigen should not be given if there is any acute illness. It has to be replaced by double antigen (DT vaccine) in children with (i) previous history of unstable neurological diseases like convulsions, progressive brain damage (ii) previous severe reaction to vaccine other than local reactions.
 - S/E: Local oedema, erythema and nodule formation, sterile abscess, encephalitis (rare) and convulsions (rare). Fever for a day is common and Paracetamol is given routinely for a day.
 - P/A: Manufactured by Bengal Immunity, Haffkine, Chowgule Hind, Serum Institute and Biologics. Ampoules and 10 dose vials.
 - Dose: Primary immunisation of children starting at 1½ month, 3 doses 0.5 mL i.m. at intervals of 1 month. Single booster dose of 0.5 mL at 18 months.
 - Cost: vial (5mL) Rs 18.00
- Storage: As stated under vaccines when stored under the prescribed conditions the vaccine may be expected to retain potency for not less than 1½ years from the date on which the potency test for the pertussis component was started.

5.4.5 Double Antigen (DT).

Prepared from diphtheria formol toxoid and tetanus formol toxoid with a mineral carrier like aluminium hydroxide.

- I: Booster dose to children above 5 years of age and children allergic to pertussis component of DPT.
 - S/E: Pain at the site of injection.
 - P/A: Ampoules and 10 dose vial.
 - Dose: 0.5mL i.m. usually one booster dose at school entry.
 - Cost: Vial (5mL) Rs 11.00
- Storage: As stated under the vaccines when stored under the prescribed conditions the vaccine may be expected to retain its potency for not less than 2 years from the date on which the potency test was started.

5.4.6 Tetanus Toxoid (TT)

Adsorption on aluminium hydroxide, aluminium phosphate or calcium phosphate improves antigenicity and adsorbed vaccine is preferable to plain vaccine. It should be given i.m.

Guidelines for Clinical Management at the Peripheral Hospitals

- I: Primary immunisation, in pregnant women, before elective surgery in unimmunised persons, potentially contaminated wounds.
- P/C: Adsorbed vaccine should not be given intradermally.
- S/E: Allergic reaction, local reaction, erythema, induration, oedema.
- P/A: Manufactured by Chowgule Hind, Haffkine, Glaxo and Serum institute. 1 dose ampule, 5 and 10 dose vial.
- Dose: Primary immunisation in combination with adsorbed diphtheria vaccine and killed Bordetella pertussis organism as triple vaccine. 3 doses of 0.5 mL 6 weeks apart, boosters at 18 months, 5, 10 and 16 years. During pregnancy two doses of TT vaccine is given at 1 month interval. If there is history of recent immunisation one dose is sufficient. Tetanus vaccine need be repeated only after 3-5 years after last reinforcing dose. Very rarely, tetanus has developed after abdominal surgery and patients awaiting elective surgery should be asked about tetanus immunisation and immunised if necessary.
- D/I: Administration to patients who are on immunosuppressants, including corticosteroids or radiotherapy, resulted in an insufficient immunisation.
- Cost: 0.5 mL Rs 2.00
- Storage: As stated under vaccines when stored under the prescribed conditions the vaccine may be expected to retain potency for not less than 2 years from the date on which the potency test was started.

5.5 OPTIONAL VACCINES

5.5.1 Mumps, Measles & Rubella (MMR)

MMR vaccine contains live attenuated measles, mumps and rubella vaccines. Lyophilised vaccine stored at $-2-8^{\circ}\text{C}$. It should be given only after 1 year of age preferably at 15 months. MMR vaccine can be given to children of both sexes even if previous measles vaccine has been given.

- C/I: Pregnancy, acute febrile illness, congenital or acquired immunodeficiency, allergy to chick egg proteins, recent therapy with steroids or immunosuppressants, active tuberculosis and hypersensitivity to neomycin, Kanamycin and documented history of MMR vaccination.
- P/C: Postpone the vaccination in patients suffering from acute illness. The disinfectant or alcohol used at the site of injection for cleansing the skin should be allowed to evaporate before injection otherwise inactivation of live vaccine may occur, pregnancy and lactation.
- S/E: Local erythema, pain and induration, regional lymphadenopathy, rash and parotitis.
- P/A: Manufactured by Serum Institute "TRIMOVAX"
- Dose: 0.5mL s.c. or i.m. into outer part of upper arm.
- D/I: Same as for MMR
- Storage: As stated under vaccines the dried vaccine may be expected to retain potency for not less than 12 months from the date of last

determinations of the virus titres. When reconstituted vaccine should be used immediately.

5.5.2 Rubella Vaccine

Lyophilised live attenuated vaccine. Cheaper than MMR vaccine. Main indication is for prevention of congenital rubella by vaccination of adolescent girls and boys.

C/I: History of hypersensitivity reaction of this vaccine or any of its components, patients receiving immunosuppressive therapy, blood dyscrasia, leukaemia, lymphoma or any type or other type of malignant neoplasms affecting bone marrow or lymphatic systems, primary or acquired immunodeficiency, persons who are immunosuppressed in association with AIDS or other clinical manifestations of infection with HIV, cellular immune deficiencies, and hypogammaglobulinaemia and dysgammaglobulinaemic states, active untreated tuberculosis, family history of congenital or hereditary immunodeficiency, until immune competence of the potential vaccine recipient is demonstrated.

P/C: Pregnancy, Vaccination is not recommended for children below 12 months of age. Defer immunisation during the course of any acute illness.

S/E: Burning or stinging of short duration at the injection site, regional lymphadenopathy, urticaria, rash, malaise, sore throat, fever, headache, polyneuritis, temporary arthralgia, local pain.

P/A: R-vac vial (0.5 mL)

Dose: 0.5mL s.c.

D/I: Same as for MMR

Cost: Vial (0.5mL) Rs 37.00

Storage: As stated under vaccines the dried vaccine may be expected to retain potency for at least 2 years when reconstituted the vaccine should be used immediately.

5.5.3 Hepatitis B Vaccine (HB)

Alum adsorbed inactivated hepatitis B, virus surface antigen prepared from plasma of human carriers: It is also prepared biosynthetically using recombinant DNA technology. Supplied as aluminium salt adjuvanted liquid. Store refrigerated, not frozen. Synthetic vaccine stable for 1 month at 37 degree centigrade. Single and multidose vials available

I: Prevention of Hepatitis B infection to infants born to HBs Ag positive mothers. In these cases the first dose should be given preferably with hepatitis B immunoglobulin. High risk patients requiring repeated blood transfusion like Thalassaemia, Haemophilia, frequent dialysis, portal hypertension, medical personnel in contact with acute hepatitis B cases, are all indication for vaccination. WHO recommends universal immunisation of all neonates in areas with high prevalence of HBV carriers. Irrespective of age, immunisation should be started

Guidelines for Clinical Management at the Peripheral Hospitals and completed in all HBsAg negative individuals, since it reduces risk of HBV carrier state, cirrhosis and carcinoma liver. Seroconversion rate is poor after the age of 40 years.

C/I: Hypersensitivity to any component of vaccine, pregnancy.

S/E: Erythema, swelling, fever, malaise, headache, dizziness, nausea.

P/C: Vaccination does not eliminate the need for the general precautions for avoiding risk of infection from known carriers by the routes of infection which have been clearly established.

Dose: 1mL(20 mcg) i.m. Avoid gluteal region. Children below 10 years 0.5mL (10 mcg.) Passive immunisation by HB Ig 0.06 mL / kg i.m. (1mL = 100 units). Plasma derived vaccine and recombinant vaccine can be interchanged though it is better to use the same vaccine for the primary course.

Recommended schedule of vaccination.

- a) primary immunisation-i.m. 2 doses of 1 mL at interval of one month and 1 mL on 6th month after 1st dose. Immunisation takes up to 6 months to confer adequate protection and duration of immunity lasts for 3-5 yrs.
- b) Booster-1 mL every 5 -10years.
- c) Children under 10 years- ½ adult dose.
- d) Larger doses of vaccine is required for persons receiving immunosuppressive therapy/immunodeficient. Inject twice the adult dose and also patients with chronic renal failure on haemodialysis.
- e) In those accidentally infected, specific antihepatitis B virus immunoglobulin should also be given
- f) Infants born to HBsAg-positive mothers: 3 doses of 0.5 mL are given at birth, 6weeks and 6 months. First dose is given at birth along with antihepatitis B immunoglobulin injection at a different site within first 12 hours of delivery. Even without HB Ig the protection rate is about 95%.
- g) If mother's immunisation status is not known HB vaccine should be given at birth without HB Ig. again at 6 weeks and 6 months. If mother is known to be a noncarrier for HB antigen then no need to give vaccination at birth. 4 doses are recommended by IAP and is given along with DPT vaccine at 6, 10 and 14 months and at 12 months. A booster dose at 10 years is also recommended by Indian Academy of Paediatrics (IAP). Double dose of vaccine should be given for patients on immunosuppressive therapy.

P/A: Engerix-B, and Shanvac-B, (Recombinant) Hepavax B and Hepaccine (plasma derived)

Cost: Vial (200iu/mL) Rs 994.00

Storage: Store in light resistant containers at a temperature between 2-8 °C. The vaccine must not be allowed to freeze. When stored under the prescribed conditions the vaccine may be expected to retain its potency for not less than 2 years from the date of carrying

out the last satisfactory potency test.

5.5.4 Typhoid Vaccine

Typhoid (TAB) Vaccine

- a) Sterile suspension of heat/alcohol killed, *S.typhi* and paratyphi A and B
- b) Oral typhoid vaccine-attenuated, *S.typhi*. Enteric coated capsules. Store refrigerated. For children below 6 years it is not recommended and they may find it difficult to swallow the capsule.
- c) Salmonella Vi antigen - Vi polysaccharide liquid vaccine, purified and adjuvenated. Not effective below 2 years.
- I: Prophylaxis against typhoid and for travellers to endemic areas. It is no substitute for personal hygiene
- C/I: Hypersensitivity to any component of vaccine or the enteric coated vaccine. Patients having immunodeficiency.
- S/E: Mild local reactions like pain, swelling, tenderness and systemic reactions like headache, fever, malaise. Intradermal injection has lower adverse reactions.
- P/A: TAB vaccine, Typhim Vi, TyphOral
- Dose: TAB vaccine: Primary immunisation 0.5 mL s.c. or i.m. Followed by 0.5 mL after 4-6 weeks, children 1-10 yrs 0.25 mL. Available with health authorities. Typhoid Vi antigen (typhim Vi) 0.5mL s.c. or i.m. single dose. Oral vaccine (TyphOral) to be taken one hour before meal with a cold drink. 1cap on alternate days for 3 days (1,3,5)
- D/I: The vaccine should not be administered to individuals receiving sulfonamides and antibiotics since these agents may be active against vaccine strain and prevent a sufficient degree of multiplication to occur in order to induce protective immune response.
- Cost: Syringe (5mL) Rs 290.00
- Storage: Store at temperature between 2-8°C. The liquid vaccine must not be allowed to freeze.

5.5.5 Haemophilus Influenza Type b Conjugate Vaccine (Hib Vaccine)

Very effective in preventing meningitis and epiglottitis caused by *H. influenza* in children. Capsular antigen b conjugated to protein antigen TT DT or Meningo OMP. Lyophilised vaccine, store refrigerated.

Each dose 0.5 mL contains 10 mcg of Haemophilus b Saccharide conjugated with protein antigen. Very effective vaccine against *H influenza* type b. But very expensive.

Recommended schedule

2-6 months 3 doses at 2 months interval 1 Booster after 1 year
Can be given with DPT at a different site

12 months	2 doses at 2 months interval	1 Booster after 1 year
5 years	1 dose	No Booster dose

P/A: Hibtiter, ActHib.

Cost: 0.5 mL Rs 473.00

Storage: As stated under vaccines. The vaccine may be expected to be suitable for use for 1 year.

6 VACCINATIONS FOR SPECIFIC PURPOSE.

All vaccines contains inactivated viruses

6.1 Rabies Vaccine

- Human diploid cell line vaccine (HDCV) Dose 1mL
 - Vaccine from chick embryo cell (PCEV) Rabipur. Dose 1mL
 - Verocell culture vaccine. (PVRV) Verorab. Dose 0.5mL
- All these vaccines are lyophilised tissue culture vaccines and should be stored between 2-8 °C

- Sheep brain tissue vaccine. This vaccine can produce severe side effects like Guillian Barre syndrome or myelitis.

Dose: 5mL for adults and 2 mL for children deep i.m. on anterior abdominal wall for 14 days. Booster after 10 or 20 days may be needed

- Rabies antisera(hyperimmune horse serum) or of human rabies immunoglobulin (Berirab/Immogam 150 units/kg). Route i.m. at a site different from rabies vaccine.. Pale yellow liquid; store at 2-8 °C
- Pre-exposure immunoprophylaxis in high risk population. eg. Veterinary Surgeons, field workers, animal handlers and those working in quarantine stations. 3 Doses -days 0, 7 & 28. Booster every 3 years.

Post exposure treatment:

Depends on class of bite. 5 injections on days 0, 3, 7, 14 and 30 are usually needed. An optional 6th dose is given on day 90 in elderly patients and in immunocompromised patients. In severe bites and bites on the face and upper limb (Type III bite -WHO) on day 0 rabies immunoglobulin (human) 20 units/kg or rabies antisera equine (40 units/kg) 1/2 the dose is infiltrated around the wound and the rest given IM in gluteal region away from the site of rabies vaccine. Local cleaning of the wound with soap and water, TT and antibiotics are also essential.

C/I: Hypersensitivity to duck egg proteins and horse serum.

S/E: Local induration, erythema, regional lymphadenopathy, neurological complication especially with sheep brain vaccine, hypersensitivity to duck egg proteins, antitoxin hypersensitivity to horse serum.

P/A: Human diploid cell vaccine, Vero rab and Rabipur .

Cost: Sheep brain suspension vial (30mL) Rs 111.00

Human diploid cell inj (2.5 iu) Rs 758.00

Chick embryo vaccine inj (2.5 iu) Rs 250.00

5.6.2 Cholera Vaccine

- a) Heat or phenol killed suitable strain of *V.cholera*
- b) Formolised cholera vaccine

I: Prophylaxis against cholera, travel to or from a country where cholera exists.

P/C: Duration of immunity last only upto 6 months. It cannot control the spread of the disease. Hence attention to hygiene, food and water is essential in endemic areas.

S/E: Fever, malaise, tenderness at the inj. Site.

Dose: Adult 0.5 mL i.m. or deep s.c. second dose after 4 weeks 1mL i.m.
child 1-5 years, 0.1 mL
second dose 0.3 mL; 6-10 years, 0.3 mL, second dose 0.5 mL; immunity appears in 7-10 days lasts for 6 months

Cost: Vial 30mL Rs 32.00

Storage : Store in hermetically sealed light resistant containers at temperature between 2-8 °C. When stored under the prescribed conditions the vaccine may be expected to retain its potency for not less than 2 years from the date of the potency test was started.

5.6.3 Yellow Fever Vaccine

Live attenuated yellow fever virus grown in chick embryo.

I: Prophylaxis-travellers to endemic areas of Africa and South America

C/I: Children under 9 months of age are more susceptible for post vaccinal encephalitis. Pregnancy, impaired immune response, sensitivity to egg proteins, immediate convalescence from other viral infections are contraindications. Do not combine it with other live vaccines.

S/E: Encephalitis (rare)

Dose: 0.5 mL of reconstituted preparation i.m./s.c. repeated every 6-10 years, immunity is established within 10 days and lasts for 6-10 years.

P/A: available with health authorities.

Storage : Store the dried vaccine in the dark at a temperature of 2-8 °C. When stored under the prescribed conditions the vaccine may be expected to retain its potency for at least 2 years. When reconstituted it should be used immediately after preparation.

5.6.4 Meningococcal Vaccine

I: Capsular polysaccharide vaccine against meningococcus A&C indicated only in specific epidemic period.

C/I: Acute infectious disease, pregnancy.

P/C: Meningitis caused by other meningococci group doesn't give protection; it should be avoided in children below 2 years

S/E: Low grade fever, pain at injection site.

Dose: 0.5mL s.c. or i.m. single dose. 95% protection. ,freeze dried . Booster every 5 years.

Cost: Vial 10 dose Rs 250.00

Storage: Store at 2-8 °C. The dried vaccine may be expected to retain its potency for not less than 12 months from the date of the last determination of the virus titres. When reconstituted vaccine should be used immediately.

5.6.5 Pneumococcal Vaccine

Pneumococcal vaccine is indicated only in specific conditions as before splenectomy where the subject is more prone to pneumococcal infection. It is effective in a single dose if the type of pneumonia in the community is reflected in the polysaccharide contained in the vaccine. Protection lasts for 5 years, but revaccination is not recommended because of the risk of adverse reactions.

Dose: 0.5mL s.c. or i.m. Freeze dried vaccine giving 85 to 90 % protection.,

Cost: Inj 0.5mL Rs 610.00

5.6.6 Japanese B Encephalitis Vaccine

Is a killed virus vaccine prepared from the Nakayama strains of Japanese -B-virus, has been in use in Japan, Korea and South East Asian countries. Vaccine is mainly for use in endemic areas and during an epidemic.

Dose : The dose is 0.5 mL ,2 doses at 4 weeks interval by intramuscular route. The use is restricted to epidemic situations only in endemic areas.

Storage : Store at temperature below 10 °C. When stored under the prescribed conditions the freeze dried vaccine may be expected to retain its potency for at least 5 years.

Cost: Not freely available.

5.6.7 Hepatitis A Vaccine

This is freely available in India now. It is a sterile suspension of formaldehyde inactivated hepatitis A virus adsorbed onto aluminium hydroxide. This is recommended for persons travelling to endemic areas where prevalence is high.

Dose : Primary course, 2 doses at 1 monthly interval followed by a booster 6-12 months later.

Adult dose 1mL, children (1-15 years) 0.5mL i.m. in deltoid region.
eg. Havrix (Smith Kline Beecham)

Storage : As stated under vaccines.

Cost : Injection 1 mL (vial) Rs. 250.00

5.6.8 Varicella Vaccine

Live attenuated vaccine, now also available in India. Lyophilised vaccine is given s.c. or i.m. 95 to 100% protection.

C/I: Pregnancy.

- S/E: Mild fever rash.
P/A: Varilix (Smith Kline Beecham)
Dose: Below 13 years single dose. Above 13 years 2 doses at 1-2months interval.
Cost: Inj (0.5 mL) Rs. 1345.00

5.6.9 Influenza Vaccine

- I: In high risk persons when an epidemic is likely to occur, elderly persons, chronic respiratory or cardiovascular diseases, diabetes mellitus, chronic renal failure, immunocompromised persons, persons with haemoglobinopathy are all high risk groups requiring vaccine prophylaxis. Vaccination is required annually due to the chance for new mutation. The vaccine strain is determined by the epidemiological consideration regarding the strain of influenza virus causing the epidemic.
- Dose: 6 months -3 years = 2 doses 0.25 mL(7.5mcg);
3 to 12 years 0.5mL(15mcg) 2 doses.
Over 12 years 0.5mL(15mcg) single dose.
- Storage: As stated under the vaccines. The vaccine may be expected to be suitable for use for 1 year. (The date after which the vaccine should no longer be used is subject to the strains of virus continuing to be appropriate).
- Cost: Not freely available.

5.7 Antisera used for passive immunisation

Before administering any of the antisera hypersensitivity is tested by an intradermal test. 0.02 mL of 1:1000 dilution is given intradermally 1:10000 is given for those with a history of allergy. If a wheal develops in 30 mts the test is positive. If there is anaphylactic reaction 0.5 mL of 1 in 1000 dilution adrenaline is given i.m. and repeated if necessary.

5.7.1 Diphtheria Antitoxin.(Antidiphtheric serum)

It is prepared by immunising horses against the toxin produced by *Corynebacterium diphtheria*. It is refined and concentrated to increase its antibody content and to remove unwanted serum proteins.

- I: Emergency prophylaxis and treatment of diphtheria.
- C/I: Antitoxin should not be given after the age of 10 yrs due to possible cardiotoxicity; It is also contraindicated in persons sensitive to horse serum.
- P/C: Tests for hypersensitivity should be first carried out.
- S/E: Local reactions like nodule or cyst formation, pyrexia, allergic reactions.
- P/A: Diphtheria antitoxin 10000 units/10mL. Manufactured by Haffkine and Bengal Immunity.
- Dose: The dose of antiserum is determined by the clinical presentation, site and the extent of membrane and stage of the disease at which

treatment is given.

Mild nasal or pharyngeal diphtheria, 800 units i.m. Moderate infection: 10,000 to 30,000 units.

Severe infection: 40,000-100,000 units are given initially i.m., and for those requiring over 40,000 units, 40,000 units is given i.m. and the rest is given by i.v. route after an interval of $\frac{1}{2}$ -2 hours.

Cost: Vial Rs 84.00

Storage : Store at temperature between $2-8^{\circ}\text{C}$ and should not be allowed to freeze.

5.7.2 Gas Gangrene Antitoxin (anti gas gangrene serum)AGGS

This contains antibodies against *Cl. welchi*, *Cl. septicum* and *Cl. edematiens*. It is prepared by immunising horses against toxins of clostridial species. The resultant antisera is refined and concentrated.

I: Infected wounds, surgery, post abortal sepsis; surgical toilet and debridement of the local part should go hand in hand with the administration of AGGS. Appropriate intensive antibiotic therapy should be instituted early.

C/I: Sensitivity to horse serum.

S/E: Anaphylaxis.

P/A: Gas gangrene Antitoxin. 4000 & 10000 units. Manufactured by Bengal Immunity and Haffkine.

Dose: Prophylactic 25,000 units i.m.or i.v. Therapeutic 75,000 units i.v. repeat double the dose if condition worsens. Tetanus toxoid and gas gangrene antitoxin are given simultaneously.

Cost: Vial Rs 100.00

Storage : Store in light resistant containers at a temperature between $2-8^{\circ}\text{C}$. Liquid preparations should not be allowed to freeze.

5.7.3 Tetanus Antitoxin (Anti tetanus serum) ATS

Enzyme refined antitetanus globulins(equine) and immunoglobulin of human origin.

I: Tetanus immunoglobulin or antisera should be used selectively in addition to wound toilet,vaccine and benzylpenicillin. When a severe tetanus prone wound occurs in a non immune or partially immune individual development of active immunity will take time. Antisera/ immunoglobulin should be considered in those who have not received active immunisation and (a) whose wound was sustained more than 6 hours before treatment was received (b) those with puncture wounds potentially heavily contaminated with tetanus spores, septic or with much devitalised tissue. A dose of adsorbed tetanus vaccine should be given at the same time as the antitetanus immunoglobulin and the course of vaccine subsequently completed.

Dose: Human Antitetanus Immunoglobulin-prophylactic immunisation

250 units i.m., children 60 units/kg. Double the dose in wounds seen after 24 hours..

Therapeutic 30-300 units/kg at multiple sites i.m.; Adult dose 2000-5000units i.m.

Tetanus Anti serum 10000 - 25000 units i.v. or 20,000 units. i.m. in multiple sites.

P/A: Tetanus immune sera. (Lyophilised) Serum Institute.

Enzyme refined antitetanus globulins equine 750iu, 1500iu, 5000iu, 10000iu, 20000iu, 50000iu.

Cost: 1500iu Rs 4.00

Storage : Same as Diphtheria antitoxin

5.7.4 Normal Human Immunoglobulin(Ig)

This contains polyclonal immunoglobulin

This has only limited use in clinical practice. Human normal immunoglobulin is prepared from pools of at least 1,000 donations of human plasma, in the liquid form or freeze dried form. It is given under exceptional circumstances i.m. for protection against hepatitis A, measles, rubella.

I: Hepatitis A: to control infection in close contacts and travellers in endemic areas. Prophylactic dose 0.02-0.04 mL/kg/bw Which gives immunological protection for 3 months and 0.06 - 0.12 ml/kg, in areas of high endemicity, repeated 4-6 months on continued exposure.

Measles: to modify or prevent attack of measles, in patients with history of convulsions and those in whom live vaccine is contraindicated.

Rubella: to lessen likelihood of infection and foetal damage in pregnant women exposed to rubella for whom therapeutic abortion is unacceptable.

C/I: Severe IgA deficiency.

P/C: Live virus vaccine should not be given until 3 months after a dose of normal immunoglobulin and normal immunoglobulin should not be given for at least 3 weeks after live virus vaccine.

P/A: Gamafine Haffkine Human normal immunoglobulin 10% and 16.5% 1 mL

Cost: Inj (1mL) 16.5% Rs 63.00

Storage :Store the liquid preparations in sealed colourless, light resistant glass containers at a temperature between 2-8 °C. Store the freeze dried preparations under vacuum or under an inert gas, protected from light in a cool place.

5.7.5 Intravenous gammaglobulin

Specialforms for i.v. administration are available for replacement therapy for patients with congenital agammaglobulin aemia and hypogammaglobulinaemia Large doses of i.v. are given in many immunologically mediated diseases such as immune thrombocytopenia, Guillian Barre syndrome and others.

Specific Immunoglobulins:

Specific immunoglobulins are prepared by pooling the blood of convalescent patients or immunised donors who have recently been specifically boosted. They are used for specific conditions such as hepatitis B, tetanus, varicella zoster and rabies. Protection with the specific immunoglobulin is immediate but lasts for only 2-3 months. Specific immunoglobulins against Hepatitis B, Rabies and tetanus are available in India and these are described above along with the vaccines. Other specific immunoglobulins include Varicella/ Zoster immunoglobulin (Z.G.) and herpes simplex immunoglobulin. They are in limited supply.

5.7.6 Anti D(RhD) Immunoglobulin

Anti D immunoglobulin is used to prevent rhesus negative mother from forming antibodies to foetal rhesus positive cells which may pass into the maternal circulation during child birth or abortion. It must be injected within 72 hours of the birth or abortion. The objective is to protect any further child from the hazards of haemolytic diseases.

P/A: Human anti D immunoglobulin 250 and 300 mcg i.m. Rhesonativ-Pharmacia; Rhesuman -Alidac.

Dose: For Rhesus negative women - 300 mcg i.m. following birth of rhesus positive infant, 250 mcg if before 20 weeks gestation. To prevent immunisation after mismatched transfusion; 5000 units capable of neutralising 40-50 mL packed red cells.

Cost: Inj 250mcg Rs 1645.00

Storage : Same as Ig.

5.8 Cold Chain

For the vaccination to be effective, the full course of potent vaccine is required. Cold chain is a system of transporting and storing vaccine at recommended temperature from the manufacturer to the point of use. This is necessary because vaccines are very sensitive to heat. The essential elements of the cold chain are: People to organise and manage the vaccine distribution, equipment to store and transport vaccine, transport facilities. Actual cold chain consists of a series of transportation links during which adequate refrigeration is required to maintain potency. A satisfactory cold chain has to be maintained at three different levels.

5.8.1 Subcentre level

Risk of cold chain failure is high at this level. Vaccinator is the most important person in monitoring cold chain at this level. No vaccine should be stored here. In order to keep vaccine safe at this level, the instructions given below should be followed. Only the required quantity must be supplied. Vaccine carrier must have frozen icepacks or the thermocol carrier should be well packed with ice. Vaccination must be given in the shade and the vaccines kept

on an ice pack or in a cup of ice. Only one vial of each vaccine is taken out at a time. Unused vials must be returned to P.H.C. the same day. Opened vials should be discarded at the end of the session. How to calculate the required quantity of vaccine: Total number of pregnant women/infants in the area X proposed coverage, X number of doses of vaccine to be given including booster dose. X vaccine administration rate. Periodicity of supply depending on the number of sessions held per month. For eg. In an area with a population 6500, birth rate of 33/1000 and IMR (Infant Mortality Rate) of 95/1000 live births, the estimated number of pregnant women and infants is calculated as follows.

Eligible:

Pregnant women: Population X B.R. = $6500 \times 0.033 = 215$; Infants = population x B.R. x (1-IMR) = $6500 \times 0.033 \times (1-0.095) = 195$. Vaccine requirements for sessions held fortnightly. T.T Vaccine $215 \times 100\% = 215$; $215 \times 2 = 430$; $430 \times 1.33 = 573$; $573:54 = 24$ doses; $24:10 = 3$ vials. The calculated amount of vaccine must be obtained from the PHC.

Now see that the amount of vaccine and diluent are the same as you have estimated. Check the expiry date. See that DTP, DT and TT and TAB are not frozen. Once obtained, the vaccines have to be carried to the subcentre. For this, various equipment are used.

1. Vaccine carrier.

2. Day carrier or a thermocol box

3. Cold box is used at district store. Place fully frozen ice packs in the carrier. Stock vaccine and diluent in the carrier. Place some packing material between the DPT vaccine and the ice. Secure the lid tightly.

Vaccine carrier used in this programme can keep the vaccine cold for two days, if the ice packs are fully frozen and lid is tightly closed. Day carrier can keep the vaccine cold only for one day.

After reaching the vaccination site precaution to be taken are:

1. Vaccination site must be a cool place.

2. Keep the vaccine carrier away from sunlight.

3. Take out only one vial at a time and close the lid immediately.

4. Wrap the vials in foil to protect from heat and light.

5. After taking out place the vials in a cup of ice.

When vaccination session is over:

1. Return all the vials to the health centre store.

2. Discard all the open vials.

3. If the ice in the cold chain container is completely melted discard polio vaccines.

4. If the ice in the cold chain container is completely melted for more than a day, throw away all the vaccines.

5. Keep a record of the vaccine administered, vaccine wasted, batch number expiry date etc.

6. If the ice in the container is not completely melted, return the

Guidelines for Clinical Management at the Peripheral Hospitals
unused vials to PHC and keep in the refrigerator. It must be kept in separate box labelled 'returned'. Put a rubber band around the vial to indicate that it was taken once. If it was not used for the third time it has to be discarded. After use, the vaccine carrier has to be kept clean and dry.

Examine for any cracks. Do not put anything heavy or do not sit on a vaccine carrier.

5.8.2 PHC level

It is the responsibility of the Medical Officer to see that the cold chain operates efficiently and effectively. His main duties being: (1) Obtain vaccine, (2) maintain equipment, (3) maintain vaccine, (4) distribute vaccine, (5) monitor cold chain, (6) train staff.

Procurement of vaccine

PHC must not hold vaccine for more than a month. Hence they have to collect vaccine every month from the district store. Medical Officer must estimate the vaccine requirement well in advance and inform the officer at district levels so that he can place orders for the right quantity of vaccine with the state officer. The manufacturer must know 9 month-1 years in advance the quantity of vaccine he must procure. ALWAYS KEEP 10% ADDITIONAL STOCK AS BUFFER STOCK FOR ANY UNFORESEEN DEMAND. As compensation of the wastage that occurs during vaccination, add 25% in case of DTP, OPV and TT and 50% for BCG and measles.

When you go to district store to collect vaccine see that

1. You have enough vaccine carrier.
2. Check the estimated need.
3. Check the date.
4. Pack it properly in vaccine carrier
5. Immediately transport it to PHC and keep it in a refrigerator

Maintenance of equipment

In the PHC equipment to be maintained are

1. Refrigerator
2. Cold box
3. Vaccine carrier.

How to maintain refrigerator

1. Stack the vaccine neatly so that air can move between the boxes.
2. Keep measles and polio vaccine on the middle shelf, so that they are away from the evaporator
3. Keep the diluent (for measles and BCG) in the refrigerator with the vaccine.
4. Keep the special box to keep returned vaccine
5. Keep plastic bottles of water or spare ice packs on the lower shelf to help the refrigerator keep lower temp in case of power failure.

6. Keep the door locked
7. Keep the refrigerator in a cool room away from direct sunlight.
8. Fix the plug permanently to socket
9. Use voltage stabiliser
10. Block the inside of the door of the refrigerator so that it will not be used for storage of vaccines.
11. Check the temperature twice daily with a dial thermometer.
12. Defrost periodically
13. Tape a sheet of paper to the outside of refrigerator, which tells any one finding the refrigerator not working.

5.8.3 District store level

Officer in charge of district store is also responsible for maintaining the cold chain. He too is involved in obtaining vaccine, maintain equipment, distribution of vaccine, monitoring cold chain and training of the staff.

Obtaining of vaccine:

Vaccine has to be collected from the state store. It may be once in a month, once in two months, but interval should not exceed 3 months. Vaccine should never be stored in district stores for more than 3 months. The amount needed is estimated and one person is given responsibility of intending, collecting, transporting, storing and distributing vaccines.

Before the vaccine is delivered

Confirm the arrival: Ensure that sufficient space for storage is available once the vaccine is delivered. Find out whether the vaccine is below 8°C during transportation.

Check the amount, Check the expiry date: Transfer the vaccine to refrigerator or walk in coolers (W.C.).

Maintenance of equipment

Type of equipment in district stores are: A refrigerator and freezer, cold box and vaccine carrier. Large district stores have walk in coolers. One person is responsible for the W.C. and any defect in W.C. should be immediately detected. It must be informed to the state EPI officer. Freezer is for preparation of ice packs, preparation of Ice, storage of polio and measles vaccine. Maintenance of vaccine. The following points have to be remembered. Do not keep vaccine for more than 3 months in district stores and more than 1 month in PHC. All vaccines are safer at temp: between +2 to 8°C for 4 months. Keep all vaccines at +2 to 8°C. If you have a freezer polio and measles can be kept in freezer. DPT, DT, TT and TAB should not be frozen. Transport vaccine in vaccine carriers or cold boxes. Check the ice packs before packing vaccine. Travel by shortest routes.

Control of vaccine stock:

Amount of vaccine at store must be known. Keep separate datewise records of vaccine receipt, distribution and balance sheet for each type of vaccine. Note the expiry date and arrival date for each batch of vaccine. Keep records of

vaccine distributed and estimated utilisation at the centres.

Distribution of Vaccine :

Before supply to PHC check the following . Requirement of PHC,
Utilisation during previous month. Estimated balanced in hand.

6. GASTROENTEROLOGY

6.1 JAUNDICE

Jaundice can be due to prehepatic, hepatic and posthepatic causes. However the most common cause in children and young adults is viral A hepatitis. If there is previous history of blood transfusions or injections, hepatitis B and hepatitis C are the possibilities. If the patient has severe body pain and hematuria or subconjunctival haemorrhage, in addition to jaundice, the possibility of leptospirosis has to be considered. Since several drugs are capable of producing hepatic damage and poly pharmacy is rampant in Kerala, drug induced hepatitis has to be kept in mind. In elderly subjects presenting with jaundice, the chance of malignancy is also high.

The management of viral hepatitis includes rest till the SGPT comes down to less than 100 units/L, low fat high carbohydrate diet, adequate hydration and avoidance of hepatotoxic drugs. During the early phase of illness an antiemetic like domperidone (10 mg t.d.s.) may be required in addition to parenteral glucose therapy. If the clinical condition is deteriorating or the jaundice persists for more than 3 weeks, the patient should be referred to a higher center for further investigations.

If the cause of jaundice is suspected to be leptospiral infection, in addition to the above supportive measures, an antibiotic like inj crystalline penicillin 10 lakh units 6 h for 1 week or doxycycline 100 mg o.d. for 1 week has to be given. Careful monitoring of renal function is very important. If there is reduction of urinary output or raising blood urea or creatinine, the patient may be referred to a higher centre.

6.2 HAEMATEMESIS

The management of haematemesis include, resuscitation, assessment of severity, empiric therapy, diagnosis of the aetiological factor and treatment.

Initially record all the vital signs including erect and supine BP and pulse. An i.v. line to be started with Normal saline and blood samples for investigations and grouping must be obtained with the venepuncture. Oxygen therapy - nasal oxygen, will help to improve the blood oxygen transport. A quick history and physical examination to be done to arrive at an aetiological diagnosis.

Presence of shock and change in postural vital signs will give clue to the severity of bleeding. Shock with systolic BP less than 90 mm Hg indicate blood volume loss of 15 - 20 %. Presence of postural hypotension suggest an intravascular blood loss of 10 - 15%. When these conditions are present, arrange for blood transfusion or packed cells.

Nasogastric tube lavage with water or cold saline can be undertaken which will decrease bleeding by vasoconstricting the smaller gastric vessels. Once the measures of resuscitation and assessment of severity are over, the patient must be referred to a higher centre for further evaluation of the aetiology of haematemesis.

A gastroscopy is to be done in all cases whenever possible to arrive at a specific diagnosis. For erosive gastritis and peptic ulcer bleeding, parenteral ranitidine 50 mg 8 h to be given in addition to oral 2 h antacid therapy. For variceal bleeding medical management include i.v. somatostatin 250 mcg bolus followed by 250 mcg per hour as infusion or i.v. vasopressin 20 units in 200 mL over 20 min. If facilities for endoscopic evaluation is available, variceal bleeding can be controlled by emergency endoscopic sclerotherapy or varix band ligation. As a last resort surgical measures like shunts and TIPSS can be tried to control variceal bleeding.

Drug management of haematemesis

Selection of the drug depends upon the cause of haematemesis.

Antacids

Antacids in a dose of 4 teaspoonful 2 h is recommended.

H₂ receptor blocking drugs

Cimetidine, ranitidine, famotidine

Proton pump inhibitor

Omeprazole, lansoprazole

6.3 GALL STONES

Management of gall stones depends upon the cause. Silent stones are better left alone since they may remain so indefinitely. When gall stones lead to severe biliary colic or secondary infection and inflammation, specific treatment is indicated.

This include analgesics, antispasmodics and antibacterial drugs.

Cholesterol stones can be treated with drugs such as chenodeoxycholic acid and ursodeoxycholic acid given orally as a long term basis and the stones may disappear.

If medical treatment fails surgical treatment is indicated.

7. CARDIOLOGY

7.1 CARDIAC ARREST

Recognition of cardiac arrest

1. Absent central arterial pulse (carotid, femoral)
2. Absence of respiration
3. Loss of consciousness.

Speed of diagnosis in cardiac arrest is critical as delay in diagnosis leads to irreversible brain damage.

Steps of cardio pulmonary resuscitation (CPR)

ABC of CPR

1. A - Airway: Open the airway using chin lift / head tilt method. Remove the dentures if any.
2. B - Breathing: Pinch the nostrils, and do mouth to mouth ventilation (if an Ambu bag is not available).
3. C - Circulation: Do a precordial thump before initiating CPR. Place the heel of one hand over the lower half of the sternum and the other hand over the dorsum of the first hand, both heels in parallel. Arms are kept straight at the elbows. Usually the rate is about 90/min. For every 5 cardiac compression, one full breath is given for 1 - 1½ seconds. If there is only one person to do cardiac compression and ventilation, do 15 cardiac compression and then 2 full breaths. The thump may help regain sinus rhythm in some cases of VF, VT and asytle.

Defibrillation

If a defibrillator is available, no time should be wasted. The paddle should be placed at the sternum and apex and first shock should be at 200 joules. If recurrence occurs, give a second shock also at 200 joules. 3rd shock should be at 300 joules and subsequently at 360 joules. For children the strength of current is 2 joules /kg. make sure that the bystanders are not touching the patient and also remove any metal parts.

Drugs used in CPR

Epinephrine or adrenaline 0.5 - 1 mg (1 mL 1/1000 solu.) i.v., repeated at 3 - 5 min or can be instilled with a injection into the tracheobronchial tree. It is preferable to avoid intracardiac injection (only if intravenous access is not available).

Other drugs that may be used include atropine (bradycardia), lignocaine, bretylium, propranolol (ventricular and tachyarrhythmias), metaprolol. Calcium chloride is specifically indicated in calcium channel blocker over dosage.

Sodium bicarbonate is not routinely recommended, though after a prolonged (>5 min) arrest 20-50 mL is to be administered i.v. as a slow bolus injection.

Management of cardiac arrest is a team work and successful resuscitation depends on close cooperation between the various medical personnel. Every effort should be made to recognise cardiac arrest immediately and start cardiopulmonary resuscitation without any delay.

Note: All the personnel working in the hospital should be trained to participate in the primary cardiopulmonary resuscitation. Once the patient has recovered, he/she should be referred to nearest higher centre with an attendant for further management.

7.2 ACUTE MYOCARDIAL INFARCTION

Diagnosis :History of prolonged typical or atypical cardiac pain lasting for 30 minutes or more. ECG changes - ST elevation, with or without q wave. Cardiac enzymes are not useful in the very early stages. In any setting, the history and ECG should enable the doctor to make a proper diagnosis.

Management :

1. Transfer to a hospital where ICCU facility is available after instituting the **primary treatment, i.e. aspirin and pain relief.**
Sublingual nitrate if BP is more than 90 mm Hg systolic.
Aspirin 150 - 300 mg to be chewed or swallowed at the earliest instance.
2. Relief of pain and anxiety
 - a. Inj.morphine 3 mg i.v. with Inj.phenergan 12.5 mg may be repeated every 5 - 10 min.
 - b. i.v. infusion of nitroglycerine 25 mg in 500 mL saline to be started at the rate of 1 drop/min and increased by 1 drop every 5 min till the systolic BP falls by 30% or to 90 mm Hg or pain is relieved.
 - c. Oxygen administration by nasal mask at the rate of 4 -6 L/min. This is started at the earliest opportunity.
3. Myocardial salvage :
 - a. Thrombolytic therapy in patients who come within 12 hrs of index pain and who has ST segment elevation of more than 1 mm in 2 consecutive leads. Inj.streptokinase 1.5 million units in 100 mL of saline is given in 45 min to 1 h as a drip. Inj.urokinase may be given in patients with contraindication to streptokinase. The aim should be to administer streptokinase as early as possible.
 - b. i.v. betablocker, metoprolol 5 mg bolus every 5 min to a maximum of 15 mg if there is no contraindication such as heart failure, heart block, bradycardia or hypotension. This has to be followed up with an oral beta blocker such as metoprolol 50 - 100 mg b.d. This reduces the risk of total arrhythmias and improves myocardial salvage.
4. Treatment of Life threatening complications:

Arrhythmias : see section on management of common arrhythmias

Left ventricular failure : Propped up position, oxygen inhalation, physiological venesection, i.v. frusemide 40 - 100 mg, i.v. morphine 3 - 5mg, i.v. aminophylline 5 mg/kg i.v. diluted with 25 mL of 25% glucose over 10 min.

Shock : i.v. fluid, dopamine infusion at the rate of 3-15 mcg/kg/min
5. Prevention of ventricular remodelling :

ACE inhibitors are started as early as possible, when the patient is stable. Captopril 6.25 mg t.d.s. is started and the dose is increased and maintained at a level where the systolic BP is maintained above 100 mm of Hg. Instead of captopril other ACE inhibitors may also be used in the normal dose.

6. Secondary prevention :

Beta blockers are started on the second day unless, contraindicated by LV failure or asthma. Aspirin which is started on admission is continued life long in a dose of 75 - 150 mg/day taken soon after meals.

7. Ambulation and discharge :

patient with uncomplicated myocardial infarction is made to sit up after 24 hrs. By third or fourth day he is made to move around in bed once or twice a day. By fifth to sixth day patient is made to walk in the room and he is discharged in 7 - 8 days. Patients with heart failure or other complications are ambulated more gradually and discharged after their conditions become stable after appropriate investigations done in a cardiology centre.

Note: Conditions like diabetes are not reason for withholding beta blockers. It is better to control the diabetic state with insulin during the initial phase of acute myocardial infarction.

7.3 CARDIAC TAMPONADE

1. Recognition of cardiac tamponade
2. Treatment of cardiac tamponade.

Recognition of cardiac tamponade

1. Clinical diagnosis
2. Confirmation by investigations.

Clinical diagnosis of cardiac tamponade is suspected when a patient has

- a. Hypotension and low volume pulse.
- b. Pulsus paradoxus.
- c. Elevated JVP (may be normal in low pressure tamponade)

A high index of clinical suspicion is required. Usual clinical situation where cardiac tamponade is encountered are

- a. Thoracic trauma
- b. Pericardial effusion - especially in chronic renal failure, malignancies, tuberculosis.

The definitive diagnosis is by echocardiography. The treatment for cardiac tamponade is immediate pericardiocentesis which is life saving. It should be done under monitor preferably in a cardiology unit. In a life threatening situation the primary care doctor should attempt pericardiocentesis by the subcostal route using a long large bore needle and 20 mL hypodermic syringe. Rush the patient to cardiac centre after tiding over the crisis.

7.4 ACUTE CARDIOGENIC PULMONARY OEDEMA

1. Recognition and treatment of precipitating condition.
2. Management of acute LVF.

Suspect acute pulmonary oedema when there is acute dyspnoea, cough, presence of cardiac murmurs, systemic hypertension, history of heart disease.

Treatment:

1. Oxygen inhalation
2. Injection morphine(low dose) 1- 3 mg 8 h i.v. may be repeated at 15 - 30 min interval. An injection of drugs like phenergan or metaclopramide may be given to reduce the incidence of vomiting.
3. Frusemide 40 - 80 mg i.v. (large doses upto 200 mg if no improvement in 30 min)
4. Intravenous nitroglycerine infusion.
5. Aminophylline infusion 2 - 5 mg/kg slowly for 20 min.
6. Intravenous nitroprusside if marked hypertension is present.
7. Physiological venesection using multiple tourniquets.
8. If hypotension is present, positive inotropic agents like dobutamine infusion may be started.

Recognition of precipitating factors like arrhythmia, infection, pulmonary embolism are important as they require proper management for the patient to recover from acute pulmonary oedema. For example, in a patient with severe mitral stenosis whose pulmonary oedema is precipitated by the occurrence of atrial fibrillation, control of ventricular rate by drugs like digoxin, verapamil is essential in the management.

7.5 ACUTE PULMONARY EMBOLISM

High index of clinical suspicion is required for diagnosis of acute pulmonary embolism. Usual clinical picture is that of an acutely dyspnoeic patient who has a propensity for development of pulmonary embolism (eg : a bed ridden elderly patient). In case of pulmonary infarction, patient may also complain of haemoptysis and pleuritic chest pain. In massive pulmonary embolism, the patient may present with syncope and hypotension.

Predisposing factors :

Prolonged immobilization, recent pelvic or lower abdominal surgery, heart failure, carcinoma, oral contraceptive, phlebothrombosis, elderly subjects, major accidents involving fractures or other injuries to long bones (especially femur), patients with thrombophilic tendency.

Clinical findings

- a. Chest pain, haemoptysis, dyspnoea- triad of symptoms
- b. Restlessness
- c. Cyanosis
- d. Hypotension.
- e. Raised JVP.
- f. Tachycardia, tachypnoea.
- g. RV S3 or RV S4 loud P2.
- f. ECG may show right axis deviation, S1Q3T3 pattern, incomplete or complete RBBB and transient rhythm changes. Echo cardiography, ventilation perfusion scans and pulmonary angiography are other investigations that may be required.

Treatment:

1. Thrombolytic therapy as for MI.

2. Treatment of underlying diseases.

3. Anticoagulation with heparin.

In primary care centres treatment involves correction of hypotension, O₂ inhalation and heparin (5000 units i.v.) and immediate transfer to a major centre.

7.6 CHEST PAIN

Acute chest pain is a common presentation in any emergency department. Prompt recognition of the cause of chest pain and correct management will result in benefit to the patient.

The most important factor in the assessment of chest pain is a proper history taken quickly. The major causes of acute chest pain are:

1. Acute myocardial infarction/angina
2. Acute pericarditis
3. Aortic dissection
4. Pneumothorax
5. Pneumonia
6. Peptic ulcer
7. Oesophageal spasm
8. Costochondritis
9. Pancreatitis

A proper history will identify the cause of chest pain in majority of cases. The next step is to do a thorough clinical examination specially looking for hypo or hypertension, inequality of pulses, pleural or pericardial rub and air entry in both sides of the chest, evidence of pulmonary congestion and rigidity over the abdomen.

The investigations which should be done immediately if available are:

1. Electrocardiogram
2. X-ray chest (P-A view)
3. Routine blood estimations (Hb, TLC, DC, ESR)
4. Cardiac enzymes
5. Serum amylase

The management depends on the clinical diagnosis. If facilities are not available patient should be referred to the nearest centre with facilities.

7.7 COMMON ARRHYTHMIAS

Broadly classified into two

- A. Bradyarrhythmias
- B. Tachyarrhythmias

7.7.1 Bradyarrhythmias

1. Sinus bradycardia

Sinus rate less than 60/min

Asymptomatic patients require no treatment

In a symptomatic patient (syncope, seizure) or a patient with hypoten

sion treatment options include :

- a. Treatment of the cause.
- b. inj. atropine 0.6 - 2.4 mg/i.v. push.
- c. Referral to a centre where facilities for temporary pacing is available.
- d. If pacing facility is not immediately available.
Inj. isoprenaline 2 -10 mcg/ min as infusion or
Inj. adrenaline 2 - 20 mcg/ min as infusion or
Inj. dopamine 5 - 20 mg/ kg/min infusion.

2.Complete Heart Block (CHB)

To be suspected in a patient with slow regular heart rate - ECG clinches the diagnosis.

- a. Treatment of the cause such as inferior wall MI if present.
- b. Symptomatic CHB or with hypotension; the same drugs and treatment as for sinus bradycardia.

After managing the emergency, transport him to a major hospital such as Medical College hospitals or district hospitals or any non Governmental hospitals where cardiology facilities are available.

7.7.2 Tachyarrhythmias

Heart rate more than 100/min; ECG clinches the diagnosis.

1. Narrow QRS complex (QRS width ≤ 2.5 divisions in limb leads of standard ECG)
2. Wide QRS complex tachycardia.

7.7.2.1 Narrow QRS complex tachycardia.

Almost always originate above ventricle (supraventricular)

a. Sinus tachycardia - rate between 100 - 150/min

Treatment of the cause such as fever, pain, hypotension drugs and others.

b. AV nodal reentrant tachycardia (AVNRT)

Relatively common, narrow QRS tachycardia of rate between 150 - 250/min.

Vagal manoeuvres like carotid sinus massage

1. Adenosine 6 mg i.v. bolus upto 12 mg
2. Inj. verapamil 5 mg i.v. as a slow push in 5 min. This may be repeated at 5 min interval upto a maximum of 15 mg.
3. Inj. diltiazem 7.5 - 15 mg i.v. in 2 - 3 min.

If there is hypotension, angina etc. - immediate DC cardioversion.

Longterm management : Oral beta blockers, diltiazem, verapamil or digoxin.

c. Wolffe-Parkinson - White syndrome.(WPW syndrome)

ECG features, short PR interval, slurred upstroke of QRS complex and paroxysmal supraventricular tachycardia. Acute management of tachycardia, same as AVNRT.

Long term therapy : amiodarone, quinidine and disopyramide may be effective - radio frequency ablation of the aberrant pathway is available

Guidelines for Clinical Management at the Peripheral Hospitals
at Sree Chitra Thirunal Institute of Medical Sciences and Technology,
Thiruvananthapuram. - This is curative in most cases.

d. Atrial fibrillation (AF)

Management : In the case of AF with rapid ventricular response, in the setting of ischaemia, myocardial infarction or hypotension it may lead to worsening of heart failure and this needs urgent DC cardioversion. In other patients with AF (both acute and chronic) control of ventricular rate is aimed at using beta blockers, diltiazem, verapamil or digoxin. Majority of patient with acute AF spontaneously revert to sinus rhythm. Pharmacological cardioversion using amiodarone may also be tried in patients with acute AF. Amiodarone is given in a dose of 600 - 800 mg/day or 200 mg t.d.s. or q.d.s. oral for 7 - 10 days followed by 200 - 400 mg/day. In emergencies it can be given as i.v. infusions through a veno caval catheter in a dose of 5 mg/kg b.d. within 20 - 120 min or as slow infusion, the maximum total dose not exceeding 1.2 g in 24 hours.

Anticoagulation is often required for chronic AF, especially in presence of heart failure and valvular heart diseases

Oral anticoagulation is given life long except for those above the age of 70 years. Warfarin 5 mg or phenindione 50 mg is started and dose adjusted according to prothrombin time results (INR to be maintained between 2 - 2.5)

7.7.2.2 Wide QRS complex tachycardia

Commonest cause is **ventricular tachycardia (VT)**

Immediate treatment - in sustained VT with haemodynamic compromise, synchronized DC cardioversion is indicated.

In stable VT :

1. Inj. lignocaine : 1-2 mg/kg i.v. bolus slowly, followed by infusion at the rate of 2 mg/min.
2. Inj. mexilitine : 150-200 mg 8th hrly, increments 50-100 in 2-3 days, maximum 1-2g/day
3. Inj. bretylium : 5 - 10 mg/kg diluted to 1:4 to be given in 8 min. This may help in resistant cases.

Long-term management :

Patients with VT not associated with acute myocardial infarction require further investigation for consideration of long-term antiarrhythmics like beta-blockers or amiodarone.

Ventricular Fibrillation (VF)

Suspect this condition in all cases of apparent cardiac arrest, i.e. the patient falls unconscious with unpalpable arterial pulsations (especially look for carotids) and absence of heart sounds. ECG confirms the diagnosis.

Management:

Immediate defibrillation with cardioverter with a current of 300 J, followed by cardiopulmonary resuscitation is indicated. If the first attempt of defibrillation fails repeat with 360J, two more times. If there

is no response repeat defibrillation after giving an i.v. bolus dose of adrenaline in a dose of 1 mg or bretylium 10 mg/kg. Once heart sounds are audible maintenance infusion of i.v. lignocaine or i.v. bretylium is given. If the cause of VF is not identifiable long term oral amiodarone is to be considered after detailed evaluation.

In any case institute primary cardiac resuscitation measures under all circumstances and send the patient to a cardiology centre as quickly as possible preferably with a trained assistant.

7.8 CONGESTIVE CARDIAC FAILURE

1. Identify the cause of heart failure.

2. Non pharmacological measures include

- a. Avoidance of smoking and alcohol.
- b. Restriction of physical activity.
- c. Restriction fluid intake to 1.5L/day
- d. Dietary salt restriction to below 2 g/day.
- e. Discontinuation of drugs with negative inotropic effect such as high doses of beta blockers, diltiazem, verapamil, disopyramide and NSAIDs.
- f. Oxygen administration if there is dyspnoea.

3. Pharmacological Measures :

a. Diuretics : to relieve symptoms :

Start with i.v. or oral frusemide 40 - 80 mg/day depending upon the clinical urgency . The dose may be increased if there are features of persistent fluid overload as evidenced by increased JVP, hepatomegaly and oedema. In patients without renal failure give potassium in a dose of 4 - 8g/day or combine frusemide with a potassium sparing diuretic such as spironolactone 25 mg b.d. or t.d.s. In unresponding cases thiazide diuretic (hydrochlorothiazide 12.5 - 50 mg/day) may be added.

b. ACE inhibitor:

In patients without renal failure (serum creatinine < 2 mg%) and stenotic valve lesions like severe MS or severe AS, oral ACE inhibitors like captopril 6.25 mg t.d.s., enalapril 2.5 mg o.d., lisinopril 2.5 mg o.d. may be started and the dose increased till BP is less than 120 mm of Hg systolic. The usual daily doses range from 75 - 100 mg for captopril, 20 mg for enalapril and 20 mg for lisinopril respectively.

c. Inotropic Agents :

1. Digoxin in a dose of 0.25 mg daily for 5 days a week in patients with heart failure. Start with 0.125 mg daily. Monitor heart rate for development of bradycardia, and increase in ectopics. Ideal is to adjust digoxin dosage based on serum levels of the drug. Keep the serum level at 0.5 - 2 ng/mL. In most hospitals in Kerala this is impracticable. So clinical and ECG evaluation has to be meticulous.

2. For short term use dobutamine infusion can be given in patients with low volume pulse and BP around 90 - 100 mm systolic. Start with a dose of 1 mcg/kg/min and increase over 1 - 2 h to 5 - 10 mcg/kg/min. This can be given continuously for 48 - 72 hrs. If the BP remains low dopamine infusion may be combined. Dopamine is given in a dose of 2.5 mcg/mg/min as i.v. infusion.

d. Antiarrhythmics:

If life threatening arrhythmia's or symptomatic arrhythmias, amiodarone may be useful.

e. Anticoagulants : As in chronic AF.

7.9 HYPERTENSIVE CRISIS

Hypertensive crisis is defined as a substantial increase in blood pressure usually with diastolic pressure over 120 mm Hg and systolic pressure generally above 180 mm Hg.

General guidelines:

Patient is to be hospitalised with monitoring of blood pressure at 30 min interval. Fluid balance, electrolytes and renal function should be assessed. Precipitous blood pressure reduction is likely to cause neurological complication, subendocardial ischaemia and may increase the risk of acute renal failure.

Specific Therapy

Sublingual / buccal nifedipine and captopril can bring down blood pressures rapidly and is useful as a first aid. Nifedipine 5 mg and captopril 6.25 mg are used.

Caution :

precipitous fall in BP. In such a situation , elevation of foot end of bed will help. Intravenous frusemide is helpful in excreting a salt load and especially in patients with cardiac disease. These two measures should be instituted as first aid in any setting. Intravenous infusion therapy may be required in extreme hypertension, encephalopathy and severe cardiac or renal failure. This requires close monitoring and should be under taken preferably in an intensive care unit.

Sodium nitroprusside

Initial infusion rate - 0.5 to 1 mcg/kg bw/min. This can be increased to 3 mcg/kg/min gradually. Should not exceed 10 mcg/kg/min. Caution in patients with renal failure. The infusion bottle and set should be protected from light. Not advisable to continue for more than 48 hours.

Nitroglycerine infusion

Preferred in patients with severe coronary artery disease, or advanced hepatic or renal insufficiency. The initial doses - 5 -10 mcg/min. May be titrated up to 200 mcg/min or more.

Esmolol

Initial bolus dose of 500 mcg/kg/min given over 1 min, followed by 50 - 300 mcg/kg/min as infusion.

Oral drugs

Oral antihypertensive drugs should be started simultaneously. ACE inhibitor, calcium channel blockers, alpha blocker, clonidine and alpha methyl dopa are chosen according to patient tolerance and acceptance. Start with small doses and gradually increase the dose allowing enough time for drug action. Salt and water status should be corrected - both fluid overload and depletion can lead to refractory hypertension.

7.10 HYPERTENSION

Hypertension affects 6 - 12 % of the adult population in India. The following guidelines are adapted from the Joint National Committee(JNC) VI report, USA, November 1997. The drug treatment of hypertension is based on severity of high blood pressure(HBP), associated risk factors and presence of target organ damage. Lowering of BP is associated with definite reduction in risk of coronary artery disease (CAD), stroke, renal failure, peripheral arterial disease (PAD).

Definitions:

Category	Systolic	Diastolic
Optimal	< 120 and	< 80
Normal	< 130 and	< 85
High Normal	130 - 139	or 85 - 89
Hypertension		
Stage - I	140 - 159	or 90 - 99
Stage - II	160 - 179	or 100 - 109
Stage - III	≥ 180 or	≥ 110

BP recorded while not on antihypertensive drugs sitting, upright posture. Two or more readings on separate visits after initial screening. If systolic and diastolic reading fall in different categories, higher category selected to classify.

Korotkoff Phase 1 - appearance of 1 st sound for systolic BP

Korotkoff Phase 5 - disappearance of sound for diastolic BP.

Risk factors and target organ damage (TOD) / clinical cardiovascular disease (CCD)**Major risk factors**

Smoking

Dyslipidemia

TOD / CCD

Heart diseases

LVH

Guidelines for Clinical Management at the Peripheral Hospitals

Diabetes mellitus

Age > 60 years

Angina

Prior MI

Prior coronary

revascularisation

Sex

(men & post menopausal women)

Family history of cardiovascular disease

Heart failure

Stroke or TIA

Nephropathy

Peripheral arterial

disease Retinopathy.

Risk categories

Risk group A :Stage 1, 2 or 3 hypertension without TOD/CCD and other risk factors

Risk group B :Hypertension (any stage) with atleast 1 risk factor excluding diabetes No TOD/CCD

Risk group C :Hypertension (any stage) with TOD/CCD and/or diabetes with or without other risk factors.

Treatment Recommendation

BP Stage	Risk group A	Group B	Group C
High Normal (130 - 139 / 85 - 89)	Life Style Modification (LSM)	LSM	Drug therapy
Stage 1	LSM upto 12 m	LSM upto 6 m	Drug therapy
Stage 2 & 3	Drug therapy	Drug therapy	Drug therapy

Life Style Modification recommended

- Stop smoking.
- Graded weight reduction for patients with body mass index (BMI) >27. Target weight (weight in kg/height in meters)to be achieved over 6 to 12 months.Aerobic physical activity - 30 - 45 min/ day (walking, slow running, outdoor accustomed activity such as gar dening, cycling and others).
- Sodium intake restricted to < 100 mEq /day. (6 g of salt)
- Maintain adequate intake of dietary potassium (approximately 90 mEq/ day.)
- Reduce dietary saturated fat and cholesterol.
- Limit alcohol to less than 30 mL ethanol, if it cannot be completely stopped.
- Adequate calcium (0.5 - 1 g/day) and magnesium (300 mg) in diet.
- Relaxation and bio-feedback excercise if possible.(Not enough evidence in literature)

Drug therapy

Considerations

Stage of BP; associated risk factors, TOD/CCD.

Once daily dosing preferred.

Agents with duration of action of 24 hrs helps to avoid night medications.

Age, metabolic side effects.

Quality of life, cost of drugs.

Choice of drug

A. Uncomplicated hypertension

- | | |
|---|---|
| Diuretics, beta blockers | : Start with low dose long acting or low dose combinations. |
| Substitute another drug from another class | If no response or troublesome side effects occur. |
| Add a second drug from a different class | If response is inadequate and the drug is well tolerated. |
| Continue adding agents from different classes | If still no response, consider referring to specialist |

B. Compelling Indication for initial choice

Diabetes Mellitus with proteinuria :ACE Inhibitors

Heart failure :ACE Inhibitors, diuretics

Isolated systolic hypertension in elderly: Diuretics, calcium antagonist.
Betablockers (Non ISA)
ACEI (with LV dysfunction)

C. Favourable effect on co-morbid conditions - preferred initial choice

1.Prostatism, dyslipidemia :alpha blockers

2.Essential tremor, hyperthyroidism, migraine, pre-operative hypertension : beta blockers.

3.Osteoporosis : thiazides.

4.Angina, atrial arrhythmia :beta blockers, calcium antagonists.

5.Renal insufficiency :ACE Inhibitors.

D. Unfavourable effects - preferably avoided.

Bronchospasm : beta blockers.

Depression : beta blockers, reserpine.

Dyslipidemia : beta blockers, diuretics.

Diabetes : beta blockers , diuretics.

2^o and 3^o heart bloc : beta blockers, calcium channel blockers.

Heart failure : beta blockers, calcium channel blockers (except felodipine and amlodipine)

Pregnancy : ACE Inhibitors, angiotensin II receptor blockers.

PAD : beta blockers.

Liver disease : methyl dopa, labetolol.

Renovascular diseases : ACE inhibitors, angiotensin II receptor blockers.

Target Blood Pressure - SBP < 140 DBP < 90

In patients with TOD/CCD - further reduction is helpful, especially in cerebrovascular and renal disease (Therapy goal is 125/75). Patients with diabetes also should have target BP of 130/85.

Systolic BP - better predictor of untoward events in elderly. Drug treatment to be closely monitored, orthostatic hypotension common. Drug interaction should be kept in mind when using combination and if patient is on other drugs especially NSAIDs, antacids and tricyclic antidepressants.

Drug therapy is to be individualised and monitored. Dosages vary between individuals, races and ethnic groups. Cost also should be taken in to account while prescribing rational combination of drugs. More than two drugs combination should be avoided.

7.11 SECONDARY HYPERTENSION

Renal hypertension is the most common cause of secondary hypertension. This may be due to renal parenchymal disease and renal vascular disease; renovascular hypertension comprises of 1-3% and parenchymal disease accounts for about 5 % of all hypertensive patients. Loop diuretics, angiotensin converting enzyme inhibitors (ACEI), calcium channel blockers, adrenergic receptor blockers and centrally acting drugs are the commonly used drugs in renal hypertension. Renovascular hypertension is potentially curable by surgery or angioplasty and hence full evaluation by specific imaging techniques is warranted in these situations. If the onset of HTN is below 25 years and above 55 years renal cause should be suspected and investigated.

ACE Inhibitors (ACEI)

ACE Inhibitors increases renal plasma flow and reduces renal vascular resistance, they reduce proteinuria, cause regression of left ventricular hypertrophy (LVH) and possibly prevents progression of renal disease by inhibiting growth factors.

- I: Unilateral renal artery stenosis (RAS), renal parenchymal disease, diabetes with proteinuria, idiopathic oedema
- C/I: Bilateral renal artery stenosis, hyperkalemia, pregnancy and lactation
- S/E: Cough (5-25%), angio oedema (0.1-0.2%), hypotension, dizziness, hyperkalemia, anaphylactic reactions in dialysis patients, rashes, altered taste, neutropenia, toxicity to the foetus leading to ACE Inhibitors foetopathy.

Drug	Dose/day
Captopril	50 - 150 mg
Enalapril	2.5 - 20 mg
Lisinopril	5-20 mg
Ramipril	2.5 - 10 mg
Benazepril	10 - 40 mg

Calcium channel blockers

They interfere with the entry of Ca^{++} into smooth muscle of resistance arterioles through 'L' (long lasting) voltage dependent channels. In patients with renal disease Ca blockers enhance renal blood flow and thus protect GFR. They do not have the adverse metabolic effects on lipid metabolism and potassium excretion. Hence these drugs are commonly used in patients with hypertension and renal failure.

Drug	Dose/day	Caution
Diltiazem	180 - 360 mg	Cardiac failure, AV Block
Nifedipine	30 - 90 mg	Severe renal failure
Verapamil	240 - 360 mg	Cardiac failure
Felodipine	5 - 10 mg	
Amlodipine	5 - 10 mg	
Nicardipine	60 - 120 mg	
Isradipine	5 - 10 mg	Cardiac failure

Beta adrenoreceptor blockers

Propranolol, atenolol, metoprolol

P/C : Hyperkalemia, cardiac failure.

Alpha adrenoreceptor blockers

Prazosin, terazosin

P/C : First dose hypotension

Centrally acting drugs

Alpha methyl dopa, clonidine

Note: In patients with renal failure combinations are preferred over maximum doses of single drug. Optimal effects can be obtained by judicious combinations and proper maintenance of fluid and salt balance.

7.12 ANGINA PECTORIS

Chronic angina can be managed routinely. Unstable angina is a situation demanding close monitoring and specialist evaluation since patients may develop acute myocardial infarction and other fatal arrhythmias. Unstable angina is diagnosed when a patient with previous effort angina has increased symptoms or has rest angina, or new onset angina

Treatment of acute attack

1. Sublingual nitroglycerine / isosorbide dinitrate.
2. Nitroglycerine spray.

Prevention of anginal attack

1. All patients with effort angina should receive betablockers (propranolol, atenolol or metoprolol) if there are no contraindications.
2. If beta blockers fail to control pain, calcium channel blocking drug can be given (verapamil, diltiazem).
3. Newer drugs like trimetazidine and nicorandil can be tried in refractory cases.

In patients with vasospastic angina, it is better to use calcium channel blockers (verapamil, diltiazem).

Patients who develop angina and do not improve with sublingual nitroglycerine should be referred to the nearest hospital with monitoring facility as they may be developing myocardial infarction and should benefit from early thrombolysis.

7.13 HYPOTENSION

When a patient present with hypotension i.e. systolic blood pressure below 80 mmHg, the first step is to ensure whether there is associated tissue hypoperfusion as evidenced by cold clammy extremities, obtunded sensorium, and decreased urine output.

The major causes of shock are:

- a. Cardiogenic
- b. Extracardiac obstruction
- c. Hypovolemic
- d. Distributive shock (septic shock, anaphylaxis, neurogenic, endocrinologic shock, toxic products) Common conditions presenting to us are cardiogenic shock due to myocardial infarction, septicemic shock, hypovolemic shock, massive pulmonary embolism and cardiac tamponade.

Steps in management

1. Take a limited history and do a rapid clinical examination to establish the etiology of hypotension and shock
2. If facilities are available do an urgent ECG and X-Ray chest and blood counts including PCV.
3. If hypovolemia is suspected, correct hypovolemia by means of volume expanders.
4. Inotropic agents like dopamine and dobutamine infusion should be started.
5. If septic shock is suspected broad spectrum antibiotic regimen along with correction of hypovolemia should be instituted. Combination of dopamine and dobutamine infusion is to be administered if the response to fluid administration alone is not satisfactory. Administration of steroids in septic shock is still advocated by some, though large scale studies have not shown adequate benefit. It is therefore left to the option of the treating doctor to use them. Once the patient has been managed initially, he/she should be referred to be nearest centre with facilities for more definitive management.

7.14 INFECTIVE ENDOCARDITIS

Suspect this condition in patients with prolonged fever if any of the following conditions exist.

- ♦ Prosthetic valves - refer to higher centre
- ♦ Previous history of endocarditis

- ♦ Diagnosed heart lesion
- ♦ Cardiac murmurs
- ♦ Drug addicts
- ♦ Embolic manifestations.

Infective Endocarditis Prophylaxis

In patients undergoing low risk procedures - such as minor surgery in non-contaminated regions. Cap.amoxycillin 3 g oral 1 h before the procedure and followed by 1.5g, 6 h after first dose. In penicillin sensitive patients, erythromycin 1 g is given orally 2 h before the procedure and 500 mg 6 h after first dose.

High risk patient or low risk patient for genito urinary procedures

Inj of ampicillin 2 g with gentamicin 1.5 mg/kg i.v., to be given 30 min before the procedure. Cap.amoxycillin 1.5 g is to be given 6 h after procedure. In patients who are allergic to penicillin, Inj. vancomycin 1 g i.v. infusion over in one hour along with the gentamicin 1.5 mg/kg 1 h given before procedure, and repeated after 8 h of the procedure.

8. RESPIRATORY SYSTEM

8.1 COMMUNITY ACQUIRED PNEUMONIA

In a normal young adult without any pre-existing lung disease the drug of choice is oral ampicillin (500 mg 6 h) or amoxycillin (500 mg 8 h) for 7 days. Alternate drugs are erythromycin or tetracycline. In young adults with atypical presentation, extrapulmonary manifestations and lack of leucocytosis drug of choice is erythromycin (500 mg 6 h) or tetracycline (500 mg 6 h) for 2 weeks to cover *Mycoplasma* and *Chlamydia*. In elderly people who are smokers and those with pre-existing lung disease suspect H.influenza and start the patient on oral ampicillin (500 mg 6 h for 10 days). Alternate drugs are tetracycline or erythromycin and their derivatives. Once the organism is isolated by gram stain or culture antibiotics may be changed according to that.

8.2 HOSPITAL ACQUIRED PNEUMONIA

Normal young or elderly host with nosocomial pneumonia organisms are usually gram positive and gram negative aerobic bacilli, the combination of choice is parenteral ampicillin (500 mg 6 h)/ cephalosporine (1g 6 h) and gentamicin (80 mg 8 h) for 10 days. Vancomycin is to be started in cases of strong suspicion of staphylococcus aureus. Elderly, heavy smoker or alcoholic with nosocomial pneumonia start on a combination of penicillin, erythromycin and metronidazole. For immunocompromised host antivirals and antifungals have to be considered on clinical suspicion. In such situations patients may be referred to a higher centre.

Once the organism is isolated by gram stain or culture antibiotics may be changed according to that.

8.3 ACUTE SEVERE ASTHMA

Acute exacerbation of asthma can progress on to life threatening severe

if not treated early. Intensification of bronchodilator regimen or a short course of corticosteroid can abort a life threatening asthma attack. In most situation patient's respiratory distress itself is an indicator of severe asthma attack. The clinical clues are use of accessory muscles of inspiration, pulsus paradoxus and refusal to recline. If FEV_1 and PEFr remain less than 40% of the predicted value after one intense treatment hospitalization is required.

Bronchodilator treatment.

Preparations :

1. Inhaled beta agonist - Sulbutamol / terbutaline 100 mcg 2 puffs every half an hour
2. Nebulizer device (wet aerosol) respirator solution sulbutamol 5 mg / mL 1 mL + 3 mL saline every 20 - 30 min.
3. i.v. aminophylline 250 mg mixed in 25 mL of 25% glucose i.v. bolus given in 7 - 10 min time repeated 6 h. (6 mg/kg bw). Maintain 6mg /kg bw in 24 hrs. Those already on oral theophylline the loading dose is best avoided.
4. Anticholinergic - inhaler / nebulizer / MDI. Ipratropium respirator solution.
5. i.v. corticosteroid - hydrocortisone 2 mg/kg bw i.v. bolus then 0.5 mg/kg bw i.v. line. i.v. hydrocortisone 200 mg stratum and repeated as required. Methyl prednisolone 125 mg i.v. 6 h. After 60 - 90 min of treatment with the above drugs if symptoms are not allevated intensive monitoring is essential as it can worsen to a life threatening attack. It is difficult to assess by clinical presentation alone. FEV_1 / PEFr is mandatory. If FEV_1 / PEFr remains less than 40 % of predicted that is acute severe asthma and the patient should be referred to a specialised centre for blood gas analysis and ventilator management. Maintain therapy with corticosteroids for 1 - 3 weeks which prevents relapse.

8.4 CHRONIC ASTHMA IN ADULTS

Classification	Long term	Quick relief
Step 4 Severe persistent $PEFR < 60\%$ Var : $> 30\%$	High dose inhaled steroid + a long acting bronchodilator like long acting inhaled beta agonist or sustained release theophylline or long acting beta agonist tablets. Oral steroids 2 mg/kg/day	Inhaled beta 2 agonist as needed
Step 3 Moderate persistent $PEFR 60 - 80\%$ Var : $> 30\%$	High dose inhaled steroid, or low dose inhaled steroid + long acting beta agonist	" "

Step 2 Mild persistent PEFR > 80% Var 20 - 30%	Inhaled low dose steroids, cromolyn or nedocromyl. Sustained release theophylline, zafirlukast or ziluton	"	"
Step 1 Mild intermittent PEFR > 80% predicted Variability < 20%	No	"	"

8.5 ASTHMA IN CHILDREN < 5 YEARS OF AGE

Step	Long term control	Quick Relief
Step 4 Severe Persistent	High dose inhaled steroid with spacer. If needed add systemic steroids 2 mg/kg/day /	Bronchodilator as needed for symptom relief upto three times a day
Step 3 Moderate persistent	Medium dose inhaled steroid with spacer OR medium dose inhaled steroid with cromolyn OR medium dose inhaled steroid with long acting theophylline	" "
Step 2 Mild persistent	Daily antiinflammatory medication	" " either inhaled cromolyn or low dose inhaled steroids
Step 1 Mild intermittent	No daily medication needed	Bronchodilator as needed for symptom relief-either inhaled short acting beta 2 agonist with spacer or oral beta 2 agonists.

8.6 CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Acute exacerbations :

1. Broad spectrum antibiotics based on culture and sensitivity
2. Bronchodilators : mentioned above

3. Oxygen inhalation
4. Mucolytics and antitussives
5. Anti inflammatory drugs : corticosteroids - controversial. A trial of steroids may be tried for 2 weeks in patients not responding to routine measures
6. Physiotherapy

Stepped care programme in COPD

Step I : Preventive - stop smoking

Step II : Bronchodilators and antibiotics.

Step III : Inhaled steroids are also added

Step IV : Mucolytics are also added and physiotherapy.

8.7 RESPIRATORY FAILURE

Respiratory failure is of two types - Type I hypoxic, normocapnoeic and type II - hypoxic, hypercapnoeic.

After taking the history and doing a proper physical examination, do the following investigations : Chest Ray, ECG and arterial blood gas analysis. Exclude cardiac failure. If the pH is < 7.25 and pCO_2 is > 50 , the patient is in severe respiratory distress and emergency intubation should be done.

If the patient is clinically stable and $pCO_2 < 50$, $pH > 7.25$ and bicarbonate is elevated, and the patient is in chronic respiratory failure, treatment for the lung disease is considered.

If the patient is unstable, and there is impending respiratory failure with fall in pH and rising pCO_2 , and if the patient is not known to have any lung disease, do a spirometry and treat any abnormality if present. If no impairment is present, intubate and mechanically ventilate. If the patient has an underlying lung disease, treat the lung condition and if there is no improvement, intubate and mechanically ventilate.

8.8 PULMONARY EMBOLISM

Patient present with acute onset of chest pain, haemoptysis or dyspnoea with or without mild fever. Prolonged immobilization, old age, deep vein thrombosis, pelvic sepsis, varicose vein are the common risk factors. High suspicion is necessary in high risk patients. In haemodynamically stable patients, after taking history, and doing a physical examination, take an ECG, chest X-ray, and do a blood gas analysis. If possible, do a perfusion lung scan. If it is normal consider other diagnosis. If the perfusion scan result comes as 'high probability' and there is a high index of clinical suspicion, assess the risk of anticoagulation. If low risk, anticoagulate. If high risk, do a pulmonary angiography and if positive, insert an IVC filter. If the perfusion scan result is 'low/moderate probability' or if the scan is abnormal with low index of clinical suspicion, assess the risk for anticoagulation. If low risk, do venography. If positive, anticoagulate. If venography is negative, do pulmonary angiography and if positive, anticoagulate. If patient is high risk for anticoagulation, do

pulmonary angiography and if positive, consider IVC filter. If patient has haemodynamically significant thromboembolism, exclude myocardial infarction, pericardial tamponade and tension pneumothorax. Give supportive treatment and assess the risk for anticoagulation. If low risk give intravenous heparin, reassess. If stable, do elective pulmonary arteriography and if positive, continue anticoagulation and consider IVC filter. If unstable, pulmonary arteriography is done as an emergency and if positive, give thrombolytic therapy and consider IVC filter or continuation of anticoagulants. If anticoagulants are contra indicated, pulmonary arteriography is done as an emergency. If positive, reassess clinical state and if the patient is unstable, consider embolectomy and IVC filter. If the patient is stable, consider IVC filter.

8.9 NEAR DROWNING

Results in reflex laryngospasm and aspiration.

Treatment:

1. Maintain airway
2. Artificial respiration and closed cardiac massage-(CPR)
3. Correction of metabolic acidosis
4. Correction of hypothermia
5. Maintain fluid and electrolyte balance
6. Oxygen therapy
7. Mechanical ventilation with positive end expiratory pressure
8. Cerebral resuscitation if needed.
9. Prophylactic antibiotic therapy : Broad spectrum antibiotics are given.

8.10 FOREIGN BODY ASPIRATION AND ACUTE PULMONARY COLLAPSE

Normal child suddenly present with dyspnoea and cyanosis, a foreign body aspiration should be suspected. Heimlich procedure to be done immediately to dislodge foreign body. After taking history and doing a proper physical examination, take a Chest X-ray. If the foreign body is radiolucent, do a flexible bronchoscopy and remove it. If the object is impacted, try using a Fogarty balloon catheter. If still unsuccessful, thoracotomy should be considered. If the foreign body is radioopaque, and if it is in the proximal bronchus, consider rigid bronchoscopy. If the object is in the distal bronchial tree, consider flexible fiberoptic bronchoscopy, Fogarty catheter, and open surgical removal in that order.

8.11 PULMONARY ASPIRATION

Aspiration is common in persons with altered consciousness, elderly patients on Ryles tube, tracheostomy patients and patients with hiatal hernia. It can be acid liquid, non acid liquid, non acid food particles or acid food particles.

Treatment

1. Supplemental oxygen
2. Mechanical ventilation with continuous positive airway pressure (CPAP)
3. Bronchoscopy
4. Pulmonary lavage
5. Prophylactic antibiotics : broad spectrum antibiotics.
6. Corticosteroids : methyl prednisolone hexahydrate
7. Pulmonary surfactant replacement
8. Maintain fluid and electrolyte balance.

12 INHALATION OF TOXIC GASES

Industrial gases, chlorine, ammonia, sulphur dioxide, old well (methane, phosphene, carbon tetra chloride)

Remove exposure

Wash the area to prevent corrosive effect

Oxygen inhalation

Look for pulmonary oedema

Antibiotics

Corticosteroids - methyl prednisolone or hydrocortisone

Follow up with X-ray chest and lung function studies.

13 HAEMOPTYSIS

Haemoptysis is defined as expectoration of blood derived from the lungs or bronchial tubes as a result of pulmonary or bronchial haemorrhage.

Common causes

1. Pulmonary tuberculosis.
2. Bronchiectasis
3. Bronchogenic carcinoma.
4. Lung abscess.
5. Mitral stenosis.
6. Pulmonary embolism

If the quantity of expectorated blood is more than 600 mL in 24 hrs or 300 mL in 12 hrs it is termed as massive haemoptysis and is life threatening.

Treatment

1. Bed rest and proper positioning.
2. Maintenance of airway, BP and pulse to be recorded every half an hour.
3. Sedation - required to relieve restlessness and anxiety (5 mg diazepam stat).
4. Cough suppressant - codeine phosphate/sulphate 30 mg 6 hrly
5. Antibiotics - broad spectrum, ampicillin 500 i.v., 8 h

6. Haemostatics - haemocoagulase and ethamsylate is found to be useful in practice. Adrenochrome and calcium are not effective but often given.
7. Blood transfusion if there is profuse bleeding. Patient to be referred to higher centres for proper diagnosis and management like microembolisation procedure.

After taking the history, do a thorough physical examination. The following investigations are mandatory.

Complete blood count, coagulation studies, blood gas analysis, biochemistry, chest X-ray, sputum examination for AFB, gram staining, sputum cytology and echocardiography. Exclude haematemesis, ENT sources of bleed and pulmonary thromboembolism.

If mild haemoptysis, treat infection if any. Bronchoscopy is indicated if

1. Patient is a smoker
2. Non smoker having an abnormal x-ray.
3. Non smoker aged > 35 years
4. Non smoker aged < 35 yrs, with normal chest X-ray and having recurrent haemoptysis.

If non smoker having normal X-ray and no recurrence, observe the patient and do regular follow up.

Haemostatics and cough suppressants are given for symptomatic relief.

Cough suppressants : codeine, pholcodiene, morphine : discussed previously.

8.14 ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

It is a syndrome characterized by high permeability pulmonary oedema and refractory hypoxemia. It is a systemic disease process causing endothelial damage in many organs. Therapy is therefore aimed at supporting all organ systems. This is not a single entity. If aggressive and energetic treatment not initiated immediately patient may end up with respiratory failure. Several conditions may lead to ARDS. In the new born it occurs due to prematurity and lack of surfactant called hyaline membrane disease. In the adult various conditions such as acute lung injury leading to ARDS.

Management:

These cases require management in a specialised unit having expertise for artificial ventilatory support. Monitoring of blood gases and acid base an critical care.

8.15 TENSION PNEUMOTHORAX

Patient present with severe dysnoea and chest pain. X-ray chest confirmatory. Immediate release of tension is necessary. Thoracostomy tube connected to under water seal must be done immediately. If the patient is in distress and ICD tube is not ready / available use a 20 gauge needle connected to a 20 mL syringe containing 10 mL of 1 % xylocaine / normal saline for

immediate drainage. When the piston is removed, the air bubbles out through the xylocaine and the tension gets relieved. After releasing the tension the patient should be transported to the nearest tertiary care centre. Once the emergency is tackled identify the underlying cause for management.

8.16 PLEURAL EFFUSION

Pleural effusion is a condition in which there is excess of fluid in the pleural space. Causes are classified as transudates (congestive cardiac failure, cirrhosis of liver, hypoalbuminemia, nephrotic syndrome etc) and exudates (sympneumonic, malignancy, TB etc). If the patient is dyspnoeic plural aspiration should be done. Plural fluid study, plural biopsy are to be done for diagnosis. Treatment depends on cause. For eg; if due to CCF, treat with diuretics. If due to TB treat with ATT. In malignant pleural effusions there is a tendency for fluid to recollect. To prevent this, a procedure called pleurodesis is done wherein some irritant substance is introduced into the pleural space to produce inflammation. Substances commonly used are talc, tetracycline, nitrogen mustard, bleomycin and corynebacterium parvum. Refer to the specialist for pleurodesis.

9. NEUROLOGY

9.1 MENINGITIS

The common causes of bacterial meningitis are *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Listeria monocytogenes* and *Haemophilus influenzae* type b. In neonates, Group B streptococcus, *Listeria monocytogenes* and Gram-negative rods are important pathogens.

9.1.1 Bacterial meningitis prior to hospitalisation

Prompt and early therapy of bacterial meningitis is associated with lower mortality and morbidity. If bacterial meningitis is strongly suspected on clinical grounds and there could be any delay in transfer to hospital, immediate treatment as given below should be started before transfer to hospital since meningococcal septicemia may be rapidly fatal.

Benzylpenicillin 60mg/kg (for all ages) up to 3 g i.v. or i.m.

For neonates, infants and penicillin allergic adults chloramphenicol is given in the following doses -

Children <1 week: 6mg/kg,

1-2 weeks: 12mg/kg,

>2weeks and adults: 15mg/kg, or

Ceftriaxone 50 mg/kg (for all ages) up to 2 g i.v.

Immediate and early hospital management

It should be remembered that a CT Scan is mandatory in all patients before LP if there is any evidence of raised intracranial tension. LP should be done only after ruling out a mass lesion by CT Scan, otherwise patients can develop brain coning which may be fatal.

After ruling out a mass lesion lumbar puncture and Gram staining of CSF should be done and blood cultures and throat swab taken.

If the patient arrives in hospital without having received high-dose penicillin it is essential that the patient receives empirical antibiotics to cover all common pathogens before these investigations are done.

9.1.1.1 Causative organism or susceptibility not yet known

Empirical therapy that covers the three most common pathogens should be instituted. The penicillin which is used to cover *Listeria monocytogenes* may be omitted in patients aged between 3 months and 15 years since this infection is unlikely in immunocompetent persons below the age of 15 years.

Cefotaxime 2 g (children: 50 mg/kg upto 2 g) i.v. 6 h, or ceftriaxone 2 g (Children: 50 mg/kg upto 2 g) i.v., 12 h for 7 to 10 days, plus either benzylpenicillin 1.8 g (children: 60 mg/kg upto 1.8 g) i.v., 4 h for 7 to 10 days, or (amoxycillin) ampicillin 2 to 3 g (Children: 50 mg/kg upto 2 to 3 g) i.v., 4 to 6 h for 7 to 10 days.

9.1.1.2 Causative organism of known identity and susceptibility

a. *Haemophilus influenzae* type b

Treatment

Cefotaxime or (amoxycillin) ampicillin in doses as given above.

Prophylaxis should be given to contacts by vaccination or rifampicin - the index case, household contacts, staff and other contacts in the child care facility which is attended by the index case. A suitable regimen is rifampicin 600 mg (neonates <1 month: 10 mg/kg; children: 20 mg/kg upto 600 mg) orally daily for 4 days. Where the index case is under 2 years, commence a full course of *Haemophilus influenzae* type b (Hib) vaccine as soon as possible after recovery, regardless of any previous *Haemophilus influenzae* type b immunisation. Unvaccinated contacts under 5 years should be immunized as soon as possible.

Corticosteroids is beneficial in aiding recovery and avoiding sequelae in those with *H. influenzae* meningitis. Dexamethasone in high doses (0.15 mg/kg q.d.s. for 4 days) should be instituted as soon as possible.

b. *Neisseria Meningitidis*

Treatment

Benzylpenicillin 1.8 g (children: 60 mg/kg upto 1.8 g) i.v., 4 h for 5 to 7 days. In patients hypersensitive to penicillin, give, cefotaxime 2 g (children: 50 mg/kg upto 2 g) i.v., 6 h or ceftriaxone 2 g (Children: 50 mg/kg upto 2 g) i.v., 12 h for 5 to 7 days.

Prophylaxis

Those requiring prophylaxis include the index case unless treated with ceftriaxone or cefotaxime, all household contacts, close contacts in childcare facility. A suitable regimen is rifampicin 600 mg (neonates <1 month: 5 mg/kg; children: 10 mg/kg upto 600 mg) orally, 12 h for 2 days.

Alternatively, where rifampicin is considered unsuitable, use ceftriaxone 2 g (children: 50 mg/kg upto 2 g) i.v., as a single dose, or ciprofloxacin 500 mg orally, as a single dose.

c. *Streptococcus pneumoniae*

Use cefotaxime or ceftriaxone.

In Penicillin-susceptible strains use benzylpenicillin 2.4 g (children: 60 mg/kg upto 2.4 g) i.v., 4 h for 10 days.

d. *Listeria monocytogenes*

Penicillin and (amoxycillin) ampicillin appears equally efficacious. The addition of cotrimoxazole is beneficial. In patients hypersensitive to penicillin, cotrimoxazole may be used alone. Therapy need to be prolonged even for 3 to 6 weeks.

Co-trimoxazole 160/800 (children: 5/25 mg/kg upto 160/800 mg) i.v., 6 h, plus either benzylpenicillin 1.8 g (children 60 mg/kg upto 1.8 g) i.v. 4 h, or (amoxycillin) ampicillin 3 g (children: 50 mg/kg upto 3 g) i.v., 6 h.

e. *Cryptococcus neoformans*

Intravenous administration of amphotericin B beginning with 0.4 to 0.6 mg/kg daily and increasing this dosage by increments to 1.0 mg/kg daily, at which point the drug may be given every second day, to a total of 2.0 to 3.0 g. An alternative is to give the full daily dose of amphotericin after just a single dose of 5 mg. The addition of flucytosine (150 mg/kg daily) to amphotericin B results in fewer failures or relapses and less nephrotoxicity. Both medication should be continued for at least 6 weeks.

9.1.2 Hospital-acquired meningitis

The following regimen is suggested, but should be modified on the basis of Gram stain and culture results.

Vancomycin 1 g i.v., 12 h (children: 15 mg/kg upto 500 mg i.v., 6 h), plus either cefotaxime 2 g (children: 50 mg/kg upto 2 g) i.v. 6 h or ceftriaxone 2 g (Children: 50 mg/kg upto 2 g) i.v., 12 h.

9.2 PYOGENIC MENINGITIS IN ADULTS

Pyogenic meningitis in adults is suspected when there is fever, headache, vomiting and the presence of signs of meningeal irritation. Rashes and hypotension indicate meningococcal aetiology. This diagnosis is confirmed by doing a lumbar puncture and examining the CSF for proteins, sugar cells and microorganisms by gram stain and culture. A properly done gram stain is very helpful in arriving at a diagnosis of the aetiological agent.

The emergency treatment includes starting parenteral antibiotics. The drug of choice of ordinary cases are i.v. cry. penicillin 20 lakh units 2 h and i.v. chloramphenicol 500 mg 6 h. Patient has to be given these drugs for a minimum of 10 days. If after 48 hours there is no clinical improvement repeat lumbar puncture, send the fluid for culture and start an injection of ceftriaxone 2g i.v. 12 h. If organism is isolated, antibiotics can be changed according to that if there is no clinical response.

Supportive measure for reducing the cerebral oedema includes i.v. mannitol 20 % 200 mL 3 times daily for the first 5 days. If the patient is very ill and deteriorating, i.v. dexamethasone 8 mg 8 h can be given in addition to the antibiotics.

9.3 TUBERCULOUS MENINGITIS

Clinically suspected when there is headache, irregular fever, signs of neck stiffness, with or without lower cranial nerve palsies. Diagnosis confirmed by lumbar puncture and CSF examination which shows elevated proteins, low sugar and lymphocytic pleocytosis.

Specific treatment to this condition is by 3 month course of isoniazid (600 mg o.d.), rifampicin (450 mg o.d.), pyrazinamide (750 mg b.d.) and ethambutol (800 mg o.d.) followed by another 3 months of isoniazid and rifampicin. Along with antitubercular drugs a six weeks course of dexamethasone, initially 4 mg i.v. 6 h followed later orally should also be given to reduce adhesion and to prevent sequelae. During the course of treatment if the patient shows signs of raised intracranial tension as manifested by persistent headache and vomiting, further investigations like CT scan to exclude hydrocephalous is required and he may be referred to higher centre.

9.4 EPILEPSY

- ♦ 3/4 th of persons with an isolated seizures never have another
- ♦ Factors increasing risk for recurring seizures include :
 - a. Evidence of structural lesion (strongest predictor)
 - b. Abnormal EEG
 - c. Partial seizure type
 - d. Positive motor paralysis
- ♦ Persons with no risk factors have only a 15% chance of a second seizure within 2 years. Persons with 2 or more risk factors have 100 % chance of seizure recurrence within 2 years.
- ♦ When a patient has been free of seizures for 2 to 3 years on antiepileptic drugs (AEDS), the need for continued therapy can be re evaluated.
- ♦ Risk factors for seizure recurrence include
 - a. Occurrence of many seizures before seizures are controlled.
 - b. More than one type of partial or generalised seizures.
 - c. Low IQ with abnormal neurological examination.
 - d. Failure of EEG to normalise during treatment.
- ♦ The risk of seizure recurrence is approximately 25 % in patients without risk factors and above 50% in patients with risk factors

- About 80% of seizure recurrences occur within 4 months of tapering drugs, and 90% occur within the first year.
- Driving should be prohibited for at least the first 4 months after starting drug withdrawal.
- Drug withdrawal should be attempted slowly. 25% of daily dosage is sealed down every five elimination half lives.

Drugs of choice

- A. First choice drugs for simple partial, complex, partial and secondarily generalised tonic - clonic seizures. Carbamazepine and phenytoin are the two drugs of choice monotherapy with either of them will produce a satisfactory long term result in approximately 80% of patients. Four new drugs have been approved by the FDA since 1993 for partial seizures. Felbamate, gabapentin, lamotrigine and topiramate. Felbamate is never used now as initial therapy, because of the risks of aplastic anaemia and liver failure.
- B. Second choice drugs for simple partial, complex partial and secondarily generalised tonic-clonic seizures. Three older drugs (Phenobarbital, primidone, valproic acid) and three new drugs (gabapentin, lamotrigine, topiramate) have been used as alternative drugs in patients failing to respond to the first line drugs. Phenobarbital and primidone have fallen from favour because of high incidence of cognitive / behavioural side effects and drug interactions. Gabapentin and lamotrigine have a 30-40% responder rate and have few drug interactions. Valproic acid is not more effective than newer agents and has more problems with serious toxicity, hepatic toxicity and drug interactions.
- C. Drugs for primary generalised tonic-clonic seizures. For primarily generalised tonic-clonic seizures, carbamazepine, phenytoin and valproic acid are highly effective. The latter has efficacy against absence and myoclonic seizures, where the former two are ineffective. Absence seizures may worsen in some patients taking carbamazepine and phenobarbital. Valproic acid is the drug of first choice for absences and/or myoclonic seizures.
- D. Antiepileptic drugs of choice of absences. Ethosuximide, valproic acid and clonazepam are the 3 drugs used to treat absence seizures and are equally effective. Ethosuximide has the fewest side effects and is the first choice drug for uncomplicated absences. It has however no efficacy for tonic-clonic or myoclonic seizures. Lamotrigine appears to be a promising new drug for absences.

Prognosis of Epilepsy with drug treatment

Satisfactory results (acceptable number or no seizures, acceptable side effects) are obtained in approximately 70% of patients with a single drug, either the initial choice or the alternative. 30% of patients will have inadequate control

despite trials of several drugs used alone. When a 2nd drug is added another 10% are satisfactorily controlled with a 3rd drug another 5 % are satisfactorily controlled. Approximately 15% of patients are not controlled after trials of 3 or more drugs. Such patients are considered medically refractory and may need surgery for epilepsy.

9.5 STATUS EPILEPTICUS

Time (min)	Action
------------	--------

- | | |
|---------|--|
| 0 - 5 | Diagnosis status on an emergent basis, observe vital signs, initiate EKG monitoring, blood gas studies, pulse oximetry. Establish i.v. line and draw blood samples for glucose, urea, electrolytes, haematology and Antiepileptic drugs (AED) levels. Give oxygen by mask and consider intubation and ventilation. |
| 6 - 9 | In adults 100mg thiamine first followed by 50 mL of 50% glucose by direct push into the i.v. In children, 2 mL/kg if 25% glucose is given. |
| 10 - 60 | <ol style="list-style-type: none"> 1. Lorazepam 0.1 mg/kg at 2 mg/min (maximum dose 8 mg) 2. Diazepam 0.2 mg/kg at 5 mg/min by i.v. 3. For all patients given diazepam and for patients who continue convulse after lorazepam, give 15-20 mg/kg phenytoin equivalent of Fosphenytoin at 150 mg of phenytoin equivalent / min in adults and 3 mg/kg phenytoin equivalent in children by i.v.. For patients who stop seizing after lorazepam a slower infusion rate at 50 mg phenytoin equivalent/min is given. |

greater than 60

1. If status doesnot stop after the above dose schedule, an additional 5 mg phenytoin equivalent/kg to a maximum dose of 30 mg phenytoin equivalent/kg is recommended.
2. If status persists, give 20 mg/kg of phenobarbital by i.v. at 100 mg/min. When phenobarbital is given after a benzodiazepine, the risk of apnoea is great and assisted ventilation is usually required. Instead of i.v. phenobarbitone i.v. diazepam drip can also be given as 100 mg diazepam diluted in 500 mL 5% dextrose and run at 40 mL/h.
3. If status persists, give anaesthetic doses of phenobarbital or thiopentone ventilatory assistance and vasopressors are virtually always necessary.

or

i.v. infusion of 4% paraldehyde in normal saline at a slow rate. Improper storage of paraldehyde results in depolymerization to acetaldehyde and the oxidation of the latter to acetic acid. As little as 7 mL of decompose paraldehyde (40-90% acetic acid) has proved fatal. Thus, only properly stored pure paraldehyde from freshly opened containers should be used. The second precaution is only

Guidelines for Clinical Management at the Peripheral Hospitals
glass syringes should be used since paraldehyde will decompose plastic syringes and tubing in less than 2 min.

or

Lidocaine 50-100 mg i.v. push if it is effective. 50-100 mg diluted in 5% dextrose 250 cc i.v. at 1-2 mg/min.

NB

1. 63 % of status epilepticus (SE) patients respond to diazepam and phenytoin. 25% of status patients are unresponsive to bolus injections of phenytoin and diazepam and require i.v. diazepam drip.
2. In about 12% of SE patients, convulsive SE continues beyond 60 min inspite of AEDS and require general anaesthesia.
3. Convulsive status must not be allowed to progress, nevertheless beyond 20 min, the transitional period.
4. Its also important to treat and correct the causes and immediate trigger of SE.

9.6 COMA

The causes of coma varies from an easily treatable condition like hypoglycemia to an invariably serious condition like an intracranial bleed. All comatosed patients may be transferred to a higher centre after maintaining airway and starting an i.v. line. If hypoglycemia is suspected, 25% glucose 100 mL may be pushed i.v.

9.7 CENTRAL NERVOUS SYSTEM TUBERCULOSIS

The drug treatment includes administration of three drugs Rifampicin, isoniazid, and pyrazinamide or ethambutol. These drugs are given for two months, followed by Rifampicin and Isoniazid or Isoniazid and ethambutol for 12 to 15 months. Streptomycin or ethambutol can be prescribed for patients not responding to the three-drug regime. The same regime is followed in tuberculous meningitis, intracranial tuberculoma and spinal tuberculosis. Short-term chemotherapy for CNS tuberculosis is not favored by most of the neuroscientists. In the presence of raised intracranial tension a short course of steroid therapy can also be tried.

Isoniazid is the single most important drug. It can be given in a single daily dose 5 mg/kg in adults and 10mg/kg in children. Its most important adverse effects are neuropathy and hepatitis. Giving pyridoxine 10 mg daily can prevent neuropathy. In patients who develop the symptoms of hepatitis or have abnormal liver function tests, INH should be discontinued. The usual dose of rifampicin is 600 mg daily for adults, 15 mg/kg for children. Pyrazinamide is given once daily in doses of 30-50 mg/kg. Rash, gastrointestinal disturbances, and hepatitis are the main adverse effects. The dosage of ethambutol is 750 to 1000 mg daily for adults; because of its tendency to produce gastric irritation, it is given in divided doses, after meals. This may cause optic neuropathy, so that patients taking ethambutol should have examinations of visual acuity.

Surgical intervention in intracranial tuberculoma is contemplated if vision or life is threatened due to a severe increase in intracranial pressure, when there is failure of response to medical therapy and if the diagnosis is in doubt. The surgical options include biopsy or excision of a mass lesion and shunt surgery for hydrocephalus. Surgical indications for spinal tuberculosis include failure to respond to conservative therapy, uncertainty in diagnosis and development of neural complications with paraplegia or localized granuloma with spinal cord compression.

9.8 CEREBRAL MALARIA

Quinine, chloroquine and related drugs are curative if the cerebral symptoms are not pronounced, but once coma and convulsions supervene, 20 to 30 % patients do not survive. Administration of large doses of dexamethasone administered as soon as cerebral symptoms appear may be life saving.

9.9 HERPES SIMPLEX ENCEPHALITIS

Acyclovir 10 mg/kg (for all ages) i.v., 8 h for 2 weeks.

Other forms of therapy: Mannitol can be given in cases of severe brain swelling with high initial CSF pressure. An adequate but not excessive amount of intravenous normal saline should be given. Anticonvulsants should be prescribed when seizures are present.

9.10 BRAIN ABSCESS OR SUBDURAL EMPYEMA

The infecting organism(s) vary with the underlying predisposing cause, but most brain abscesses are polymicrobial with microaerophilic cocci, and anaerobic bacteria predominating. *Nocardia* and *actinomyces* species are other causative agents. However, where the likely site of origin is the ear, enteric gram-negative bacilli are commonly involved, while after trauma or surgery *Staphylococcus aureus* must be considered.

Benzylpenicillin 1.8 g (children: 60 mg/kg upto 1.8 g) i.v. 4 h, plus metronidazole 500 mg (children: 12.5 mg/kg upto 500 mg) i.v., 8 h, plus either cefotaxime 2 g (Children: 50 mg/kg upto 2 g) i.v., 6 h or ceftriaxone 2 g (children: 50 mg/kg upto 2 g) i.v., 12 h.

In the postoperative brain abscess, substitute penicillin and metronidazole with vancomycin 1 g i.v., 12 h (children: 15mg/kg upto 500 mg i.v., 6 h).

Cases with raised intracranial tension should be managed with intravenous mannitol and dexamethasone 6 to 12 mg 6 h. The steroid can be withdrawn after 4-5 days. The duration of treatment depends on clinical response and radiological evidence of resolution. However, usually 3 weeks treatment may be necessary. Surgical management included aspiration, drain, cure and excision.

9.11 TOXOPLASMA ENCEPHALITIS/ABSCESS

In acquired immunodeficiency syndrome, cerebral infection with *Toxoplasma gondii* is common. Sulfadiazine 1 to 1.5 g (children: 50mg/kg upto 1.5 g) orally or i.v., 6 h, plus pyrimethamine 100 to 200 mg (children: 2mg/kg upto 100 mg) orally, then 25 to 50 mg (children: 1mg/kg upto 25 mg) orally, daily.

For patients allergic to sulfonamides, substitute for sulfadiazine, clindamycin 600 mg orally, 6h.

Folinic acid 15 mg orally, o.d. is usually added to reduce bone marrow suppression. Duration of therapy is for 3 to 6 weeks depending upon clinical response. Relapse is common, so maintenance therapy with half the above dosages is necessary while the patient is immunosuppressed.

9.12 NEUROSYPHILIS

Penicillin G 18 to 24 million units daily (3 to 4 million units 4 h) for 14 days.

Erythromycin and tetracycline in doses of 0.5 g 6 h for 20-30 days are suitable substitutes in patients who are sensitive to penicillin.

Lightning pains in tabes dorsalis respond to carbamazepine. Analgesics may be helpful but opiates should be avoided. Atropine and pheonothiazine derivatives are useful in the treatment of visceral crisis.

9.13 CEREBROVASCULAR OCCLUSIVE DISEASE

The disease spectrum of stroke includes transient (less than 24 hours) or reversible (less than 3 days) clinical symptoms of ischemia (TIA and RIND respectively) with temporary focal neurologic dysfunction in which there is complete recovery between or following the spells. Ischemic stroke results in a permanent focal functional neurological deficit referable to the region of brain infarction. Once a thrombotic stroke has developed fully (i.e. the completed stroke) no measures so far devised have proved to be consistently effective in restoring the damaged cerebral tissue or its function. One's efforts, therefore, must be directed to making a diagnosis of thrombosis at the earliest possible stage and circumventing the full catastrophe by all means available.

Modification of risk factors is important in the management of stroke. This includes management of hypertension, diabetes, hyperlipemia and discontinuing smoking. Heart diseases that can lead to stroke like atrial fibrillation, valvular heart diseases; myocardial infarction and congestive cardiac failure should be treated.

Antiplatelet therapy with Aspirin is indicated in the presence of TIA and RIND or previous stroke. The optimal dose of aspirin is controversial. However, several studies have confirmed the beneficial effect of low dose (75-mg daily) of aspirin therapy. There are those who advocate still larger dosage either 150 mg or 300 mg daily. Ticlopidine (250 mg b.d.) is a newer antiplatelet agent that has been shown to be beneficial in the prevention of stroke. At the present time

ticlopidine is reserved for those patients who continue to have ischemic symptoms while on aspirin therapy. Evidence is lacking that other antiaggregant drugs; notably dipyridamole and sulfinpyrazone are beneficial.

None of the cerebral vasodilators has proved beneficial in stroke prevention or management. Vasodilators may be harmful, since by lowering the systemic blood pressure or dilating vessels in normal brain tissue they may reduce intracranial blood flow.

Tissue plasminogen activators (recombinant t-PA and streptokinase) when administered intravenously convert plasminogen to plasmin, which hydrolyzes fibrin, fibrinogen and other clotting factors. Thrombolytics injected intra-arterially can dissolve occlusions in intracranial vessels. However, the incidence of intracranial hemorrhage is high in many studies. The present practice is to administer these drugs to those patients who present for treatment within 3 hours of stroke with CT evidence of no intracranial hemorrhage.

Anticoagulation therapy with Warfarin and Heparin has been used extensively to prevent TIAs and impending stroke. It is seen that the administration of anticoagulants is not of great value once the stroke is fully developed. Also anticoagulant therapy is contraindicated in the presence of CT evidence of intracranial hemorrhage. The two situations where the immediate administration of heparin seems beneficial are fluctuating basilar artery thrombosis and an impending carotid artery occlusion from thrombosis or dissection. The other clinical situation where possible need for immediate heparinisation is cardioembolic cerebral infarction. In this clinical situations heparin is given intravenously, beginning with a bolus of 100units/kg and then by continuous drip (1000 units/hour) and adjusted according to the partial thromboplastin time (PTT). Heparin therapy is maintained for several days while warfarin therapy is instituted, and the latter may be continued for several months. Warfarin can be used alone from the beginning when TIAs occur less than once every few days. Warfarin therapy, beginning with a dose of 10 mg daily, is relatively safe provided that the prothrombin activity is controlled between 15 to 17 s. The greatest usefulness of warfarin is in the first 2 to 4 months following the onset of ischemic attacks; after that the risk of intracranial hemorrhage increases greatly. Bleeding into any organ can occur when the PTT is much greater than 2.5 times the preheparin PTT. When this happens it is preferable to discontinue the heparin, check the blood clotting values and then reinstitute the infusion at a lower rate.

9.14 CEREBRAL OEDEMA AND RAISED INTRACRANIAL PRESSURE

In the first few days following massive cerebral infarction, oedema of the necrotic tissue may threaten life. In such instances, controlled ventilation should be initiated. Intravenous mannitol in doses of 1g/kg, then 50 g every 2 or 3 hours or glycerol in oral doses of 30mL every 4 to 6 hours may forestall further deterioration. Corticosteroids are of little value.

Surgical Intervention

Arterial stenosis or an ulcerating arterial plaque in the neck and thorax

of patients with recurrent ischemic attacks is usually amenable to surgical management, employing thromboendarterectomy or bypass grafts. It is found that carotid endarterectomy for symptomatic lesions causing severe degrees of stenosis (>70 percent reduction in diameter) is effective in reducing the incidence of ipsilateral hemispherical strokes. The region that most often lends itself to such therapy is the carotid sinus. Other sites include common carotid, innominate, and subclavian arteries. Balloon angioplasty and stenting of carotid artery can achieve good results.

9.15 RAISED INTRACRANIAL TENSION

Intracranial tension (ICT) is raised in several conditions such as meningitis, encephalitis, tumours, haematomas, brain oedema secondary to trauma or tumour, hydrocephalus and venous thrombosis. Raised intracranial pressure disturbs brain function by reducing cerebral blood flow and by brain herniation through the tentorial incisura or the foramen magnum. The goals of treatment are to reduce intracranial pressure in order to increase cerebral blood flow and prevent and relieve herniation.

If the cause of increased intracranial pressure is a tumour or mass lesion like haematoma, removal or decompression is the radical treatment to reduce intracranial pressure provided the lesion is accessible and operable. If the cause of increased pressure is hydrocephalus, drainage of cerebrospinal fluid by intermittent or permanent drainage is the treatment of choice. If the increased pressure is due to oedema or increased brain tissue fluid content, steroids and hypertonic solutions are of value. Alterations in the volume of blood in the intracranial space contributes to the rise and fall of ICT hyperventilation with correction of anoxia and hypercarbia relieves intracranial vasodilation. Elevation of the head above the torso favours venous drainage.

If surgery is deferred due to any reason and during the waiting period for surgery and while transporting the patient to a neurosurgical centre, medical management may have to be initiated.

The first step in the management of intracranial pressure is to quieten the patient, since movements of any type or straining frequently further elevates the intracranial pressure. Tranquilizers may be required. In some cases muscle relaxants have to be given and patient ventilated mechanically.

Patient positioning is also important. The head should be elevated at 20 degrees to ensure adequate venous drainage.

Hypertonic Solutions

These include mannitol, glycerol, urea solutions, and sucrose solutions. Of these 20 % mannitol is the most widely used. They relieve cerebral oedema. Hyperosmolar agents may also inhibit CSF formation.

Osmotic gradients between brain and plasma disappears after a short period of time because the administered osmotic solute crosses the blood-brain barrier. This results in rebound oedema. Therefore the effects of hypertonic solution is only temporary and rebound oedema may occur.

Mannitol ✧

Mannitol is not metabolized significantly when given rapidly i.v. and is excluded from the CSF and brain since it does not cross the blood-brain barrier. Therefore the chance for rebound oedema is less. Other properties of mannitol include its ability to decrease CSF production. Mannitol possesses antioxidant properties, which offers benefits on cell membrane metabolism. Mannitol also increases cerebral blood flow and cerebral oxygen consumption. This effect is independent of its action on intracranial pressure. Mannitol also acts as an osmotic diuretic.

- I: Brain oedema, glaucoma
- C/I: Congestive heart failure.
- P/C: Serum osmolality, electrolytes and urinary output should be monitored during its use.
- S/E: The increase in blood volume may precipitate cardiac failure and the loss of electrolytes can cause arrhythmias such as tachycardias. Severe hyperosmolarity can lead to renal dysfunction.
- P/A: i.v. infusion 20%.
- Dose: Mannitol 20% is given in a dose varying between 0.25 to 1.0 g/kg/bw by rapid i.v. infusion. Maximal effect is obtained at about 90 min after injection and remains so for 4 h. Because of the possibility of rebound oedema, the smallest effective dose should be used. The current practice is to administer smaller doses at frequent intervals in as short a time as possible. 100-150 mL of 20% solution is given by rapid i.v. infusion within 10 min using a large cannula. The dose may have to be repeated 4 h.

The osmotic effect of mannitol can be prolonged by the administration of frusemide given after the mannitol infusion in a dose of 0.7 mg per kg (20-40 mg).

Mannitol may increase the intracranial pressure initially for a short period on account of its vasodilator effect. This transient increase in intracranial pressure can be allayed by the administration of 40 mg frusemide 15 min before the administration of mannitol. In practice, when the intracranial tension is high, administration of frusemide 15 min prior to mannitol infusion and 30-60 min following infusion is found to be more effective.

Hyperventilation

Hyperventilation is one of the most effective means of controlling increased intracranial pressure. It achieves its effect by reducing cerebral blood flow and cerebral blood volume. Many patients with increased intracranial

pressure spontaneously hyperventilate, but sometimes intubation and ventilation may be necessary. PaCO_2 should be reduced to 25-30 mm Hg. If the PaCO_2 is reduced below 20 mm Hg, the blood flow decreases so low so much as to impair metabolic activities.

Glaucoma

In glaucoma as an emergency measure and before surgery, up to a maximum of 500 mL of 20% mannitol is given by slow i.v. infusion until the intra-ocular pressure is satisfactorily reduced.

D/I: Concurrent use of digitalis with mannitol may aggravate digitalis toxicity. Diuretics potentiate beneficial effect of mannitol

Cost : Mannitol 20% (350 mL) Rs. 87.00 - 103.00

Glycerol ☆

Glycerol unlike mannitol is partially metabolized and has a high caloric value. An advantage of glycerol is that it can be given both orally and i.v.

I: Brain oedema, glaucoma

S/E: Haemolysis, haemoglobinuria, renal failure, and hyperosmolar coma. Because of its sweet taste, it may induce nausea and vomiting when given orally.

P/A: Solution 50%

Eye drop 100%

Dose: Orally 0.25 to 2 g/kg/b.w. every 4 h. (15 to 30 ml 4th h)

D/I: Intraocular pressure reducing effects of glycerol may be potentiated by diuretics when used concurrently.

Cost : 100 g Rs. 40.00

Furosemide ☆

This is primarily a diuretic employed to eliminate salt and fluid. It has got action to reduce cerebral oedema in intracranial tension. In contrast to osmotic agents, which are effective only where the blood-brain barrier is intact, furosemide decreases brain edema in the pathological areas as well, even though the blood-brain barrier is deranged.

I: Cerebral oedema

Cortico steroids

Glucocorticoids reduce brain oedema by various mechanisms.

I: Brain oedema especially in gliomas and secondary deposits. It is not effective in traumatic lesions.

Dose: Dexamethasone 10 mg loading dose and 4 mg q.i.d..

Acetazolamide ☆

Acetazolamide inhibits carbonic anhydrase, thus reducing CSF production and consequently intracranial tension.

(For its role in treatment of glaucoma)

Dose: Oral 0.25 to 1 g in divided doses.

9.16 INTRACRANIAL HAEMORRHAGE

Primary hypertensive ("spontaneous") intracerebral haemorrhage, ruptured saccular aneurysm and vascular malformations and hemorrhage associated with bleeding disorders account for most of the hemorrhage that present as stroke.

The management includes general management of a comatose patient since most of the cases will be unconscious with maintenance of ventilation, use of controlled hyperventilation to a PCO₂ of 25 to 30 mmHg. The management also included that for raised intracranial with intravenous mannitol and frusemide along with anticonvulsant preferably phenytoin. The fluid intake should be limited 1200mL/day given as intravenous infusion of normal saline. Rapid reduction of hypertension should be avoided. A reasonable target would be a mean arterial pressure of 100 to 120 mm of Hg. Propranolol (20 to 40mg 6 h) hydralazine (10 to 25 mg 6 h) or labetalol (200 to 400 mg/day) are the most frequently prescribed oral antihypertensives. Patients who are unable to take oral medications may require parenteral hydralazine (10 to 25 mg 4-6 h). Patients with markedly elevated or unstable arterial pressure may require continuous intravenous infusion of labetalol or sodium nitroprusside.

Surgery may not benefit the comatose patients with large haematoma especially those involving the ventricles. Young patients with secondary deterioration and those with cerebellar haematoma are those who benefit with surgical intervention.

9.17 SUBARACHNOID HAEMORRHAGE

In the case of subarachnoid haemorrhage apart from the above medical management nimodipine 60 mg 4 h may be given immediately after diagnosis to prevent vasospasm. These cases need urgent neurosurgical consultation since early surgical intervention can prevent a fatal second bleeding.

9.18 BELL'S PALSY

Protection of the eye during sleep, massage of the weakened muscles and a splint to prevent drooping of the lower part of the face are the measures generally employed in the management of Bell's Palsy. The administration of Prednisolone (40-60 mg/day) during the first week to 10 days after onset may be beneficial. A course of NSAID can also be given.

9.19 GUILLAIN-BARRE SYNDROME

The essential point in the therapy of acute, severe cases is respiratory assistance and careful nursing. Other major part of therapeutic regimen are support of blood pressure by volume infusion and vasopressor agents and prevention of electrolyte imbalance, gastrointestinal haemorrhage, and particularly pulmonary embolism by use of subcutaneous heparin or pneumatic compression boot.

If the patient shows a significant reduction in vital capacity or severe oropharyngeal weakness, plasma exchange is instituted. This regimen removes a total of 200 to 250 mL/kg in four to six treatments on alternate days. The usual replacement fluid is saline and 5 percent albumin.

Intravenous administration of immunoglobulin (0.4 g/kg per day for 5 consecutive days) is as effective as plasma exchange.

Corticosteroids are no longer recommended as routine treatment for acute GBS.

9.20 MIGRAINE

Abortive therapy

1. Ergotamine (sublingual) : 1 tab at onset, then every half hour (max.3)
Note : not more than 10 mg of ergotamine in one week
2. Ketorolac : 5 - 30 mg oral
30 - 90 mg i.m.
3. Dihydroergotamine - 45 : 1 mg i.m or i.v. at onset repeat 30 min.
Maximum 2 mg i.v. , 3 mg i.m.
4. Dihydroergotamine nasal spray : 1 spray each nostril at onset and repeat once.
5. Sumatriptan : 6 mg s.c or 25 - 100 mg orally
Note : Sumatriptan should be delayed for 24 hrs after the past dose of ergotamine.
6. Aspirin : 650 mg every 4 h
7. Acetoaminophen : 650 mg every 4 h
8. Ibuprofen : 400 - 800 mg t.d.s.
9. Indomethacin : 50 mg t.d.s.
10. Naproxen : 500 mg b.d.

Abortive therapy antiemetics

1. Metaclopramide : 10 - 15 mg orally or i.v.
2. Prochlorperazine : 5 -10 mg orally or i.v.
3. Chlorpromazine : 10 - 25 mg orally, 12.5 mg i.m.
4. Promethazine : 50 mg orally
5. Diphenhydramine : 50 mg orally or 25-50 mg i.v.

Prophylatic therapy

Principles

Used for more than 2 attack / month that cannot be controlled with optimum abortive therapy.

Choose the drug with highest benefit / risk ratio.

- ♦ Inform the patient about the latency to benefit and the side effects.
- ♦ Avoid previously unsuccessful medications.
- ♦ Try each drugs for atleast 2 months.
- ♦ Use a headache diary
- ♦ Begin at a low dose and advance to maximum tolerated dose.

1. Beta blockers

a.Non selective	Propranalol	: 20 mg t.d.s.
	Nadalol	: 50 - 160 mg daily
	Timolol	: 10 mg b.d.
b.Selective	Atenolol	: 100 o.d.
	Metoprolol	: 200 mg (sustained release) daily.

Avoid beta blockers in

1. patients with a prolonged aura.
2. severe focal neurological symptoms, because these are reports of migrainous stroke in such instances.

	<u>Dose range</u>	<u>Frequency</u>
2. Methysergide	4 -8 mg	o.d.
3. Cyproheptadine	4 - 16 mg	t.d.s.
4. Amitryptiline	10 - 15 mg	h.s.
5. Diralproex	50 - 100 mg	t.d.s.

10. NEPHROLOGY

10.1 ACUTE RENAL FAILURE

Pre-renal and incipient ARF can be recognized by the clinical setting, clinical features of hypovolemia, presence of oliguria with production of concentrated urine of high specific gravity, osmolality and high urinary urea and creatinine content. The urinary sodium loss will be less than 20 mEq in the presence of hypovolemia. The objective of treatment is to restore fluid volume, enhance urine flow and ameliorate renal ischaemia.

Fluid replacement :

Assess degree of fluid loss by clinical criteria and /or by monitoring the central venous pressures. In fluid losses, the preferred replacement fluid is normal saline. Avoid using dextrose. In haemorrhage the ideal replacement is with blood. In burns and third space sequestration one third of the fluid replaced is preferred as plasma or one of its colloid substitutes. The common plasma substitutes used are dextran and hydroxyethyl starch. The fluid replacement is aimed at maintaining a central venous pressure (CVP) of more than 8 cm of water.

Enhancement of urine flow :

This is achieved by timely administration of loop or osmotic diuretic after fluid replacement.

Furosemide

Furosemide inhibits $\text{Na}^+\text{K}^+\text{Cl}^-$ co-transporter and reduces the metabolic requirement compromised tubule thus offering some protection from injury. In addition furosemide increases urine flow which facilitates flushing of the tubules removing obstruction. Furosemide can alter tubuloglomerular feedback and increase glomerular filtration rate (GFR). Furosemide has vasodilatory action through increased production of prostaglandins. It helps in conversion of oliguric ARF to non-oliguric ARF. The drug is administered i.v. in early incipient ARF, preferably as infusion in doses of 100 to 500 mg for its optimum effect. It is of no value in established oliguric ARF.

Mannitol

I: It is an osmotic diuretic, which increases renal blood flow. It decreases oedema of the tubular cells damaged by hypoxic insults. Mannitol decreases flux of calcium into the mitochondria of cells, and also acts as a free radical scavenger. If used early, after volume repletion it could prevent ATN.

Dose: 1 g/kg/bw as a 20% solution to be given as i.v.; not to exceed 200 g in 24 h; test dose of 200mg/kg/bw initially as rapid infusion.

Increasing renal blood flow

Inotropic agents by enhancing cardiac output can increase renal blood flow but most of these agents are also potent vasoconstrictors which ameliorates the potential benefit. Dopamine and dobutamine in low doses can selectively enhance renal blood flow by stimulation of the dopaminergic receptors.

Dopamine

I: Oliguria persisting after replenishing intravascular volume.

P/C: Avoid in hypovolemia.

Dose: 1 - 4 mcg/kg/min as i.v. infusion given for a period of 24 - 48 h. Of no value in established ATN.

Dobutamine

I: Same as above

Dose: 2.5 - 5 mcg/kg/min for 24 - 48 h.

Management of established ARF

If a patient does not respond to fluid replacement and diuretic challenge he should be referred to a centre where dialysis facilities are available. The objective of treatment is to support the patient during the period of shut down - prevent fluid overload and pulmonary oedema, hyperkalemia, ameliorate acidosis and decrease catabolism. Conservative measures include fluid restriction to 600 mL + previous days output, low protein, high caloric diet, control of infections with appropriate antibiotics, control of blood pressure, prevention of gastric erosions and GI bleed with prophylactic use of H_2

antagonists. Hyperkalemia is treated with bolus intravenous injections of calcium gluconate (10mL of 10% solution), sodium bicarbonate (30 to 50 mL of 7.5 % solution) and dextrose insulin infusion (100 mL of 25% dextrose with 8 iu of plain insulin). Drugs which are excreted mainly by the kidney should be avoided or given in modified doses. Drugs which can increase extra cellular potassium such as ACE inhibitors, NSAID and betablockers are contraindicated.

In established ARF, early institution of dialysis is recommended in order to prevent complications and reduce morbidity and mortality. Hyperkalemia, metabolic acidosis, fluid overload and pulmonary oedema, uremia, encephalopathy and pericarditis are absolute indications for dialysis.

10.2 ACUTE GLOMERULONEPHRITIS (AGN)

Post infectious glomerulonephritis is the commonest type of AGN encountered in clinical practice. Commonly encountered in children between 3-10 years. Presents acutely with oliguria, oedema, haematuria, proteinuria, hypertension and varying degrees of renal failure.

Management

Fluid overload

Restriction of salt and water.

Loop diuretics - Oral frusemide 20 - 120 mg b.d. or i.v. 1 - 3 mg/kg.

Control of hypertension.

Preferred drugs are vasodilators (calcium channel blockers, prazosin or alpha methyl dopa). Avoid ACE inhibitors in renal failure due to the risk of hyperkalemia. For treatment of hypertensive encephalopathy, refer to the section on hypertensive crisis. Dialysis support is required only in 1-2 % of cases.

Specific therapy for streptococcal infection.

Benzathine penicillin - single i.m. injection of 1.2 million units or half the dose in children.

Alternatively, oral benzyl penicillin 2,00,000 units every 6 h for 7 - 10 days.

Erythromycin (250 mg every 6 h for 7 -10 days) in patients who are allergic to penicillin. Recovery is the rule and usually all abnormalities disappear within 6-8 weeks. If resolution of abnormalities occur, no long term sequelae are seen. If symptoms persist beyond 3 months, expert opinion may be sought. Steroid therapy is not recommended without histological proof.

10.3 URINARY TRACT INFECTIONS

Bacterial infection may be defined as that condition in which bacteria are established and multiplying within the urinary tract. Diagnosis is by demonstration of significant bacteriuria on urine culture i.e. greater than 100,000 colonies/mL in clean voided midstream urine. If urine is obtained by suprapubic puncture in infants and children any colony count is significant. Women are

more likely to acquire infection than men. Even a single episode of urinary tract infection (UTI) and in young and adolescent males and children below 2 years, warrants evaluation. Recurrent episodes of urinary tract infection in women also indicates need for investigation.

For the purposes of management UTI can be categorised as asymptomatic bacteruria, uncomplicated lower and upper UTI, complicated UTI and recurrent UTI. Presence of complicating factors such as obstruction, stones, vesico ureteric reflux (VUR), systemic disease such as diabetes mellitus, sickle cell disease or trait, analgesic abuse, or immune suppression constitute complicated UTI.

Relapse is defined as the recurrence of bacteriuria with the same organism within 3 weeks of completing treatment and usually occurs in complicated UTI. Reinfection is defined as eradication of bacteriuria by appropriate treatment, followed by infection with a different organism after 7-10 days.

80% of community acquired acute infections are due to *E.coli*. *Staphylococcus saprophyticus* is the second most common pathogen. *Klebsiella*, *proteus* and *enterococci* are much less common. In hospital-acquired infections, there is an increased incidence of *klebsiella*, *proteus*, *Pseudomonas aeruginosa* and other enterobacteriae.

10.3.1 Infections of the lower urinary tract

No treatment is needed in non-pregnant women with uncomplicated asymptomatic bacteruria. In pregnant women, the risk of development of upper tract infection in the IInd and IIIrd trimester is three fold and hence treatment is necessary. Treatment reduces the development of subsequent upper urinary tract infection to less than 5%. Complicated asymptomatic bacteruria in patients with structural anomalies of urinary tract, diabetes, sickle cell disease, analgesic abuse etc. need treatment. Acute cystourethritis is also treated in the same manner. Prophylaxis is indicated if there are 3 or more relapses or reinfections within 6 months and in patients with complicated UTI.

Treatment

Nitrofurantion

I : First line treatment for asymptomatic bacteruria and uncomplicated lower tract infection.

Dose: Acute uncomplicated infection: 100mg b.d. with food for 5 to 7 days.

Children: 5-7mg/kg /day in divided doses.

Recurrent infection: 100 mg every 6 h with food for 7 to 10 days.

Prophylaxis: 50 to 100 mg at h.s.;

For children: 1mg/kg.

Drug choice should depend on local antibiotic sensitivity, cost and patient tolerance. It is preferable to avoid quinolones and nitrofurantoin in children. Routine of alkalinisation or acidification

of urine is not recommended. However alkalinisation is beneficial in recurrent E.coli infection and acidification in infection with proteus.

Nalidixic Acid

I: A 4 - Quinolone derivative effective in lower UTI.

Dose : 1 g every 6 h for 7 days.

Chronic or reccurent infection 500mg 6hrly for 2 to 3 weeks,

Children 55mg/kg /day, in divided doses 6th hrly.

Trimethoprim : 200 mg b.d. for 5 to 7 days. Avoid in I trimester of pregnancy

Trimethoprim + sulphamethoxazole (Co-trimoxazole)

160/800mg b.d. for 5 to 7 days. Avoid in I and III trimester of pregnancy

Ciprofloxacin : 250mg b.d. for 5 to 7 days. Avoid in children.

Norfloxacin : 400 mg b.d. for 5 to 7 days. Avoid in children

Ampicillin : 500 mg 8 h for 5 to 7 days.

Children : half adult dose.(50-100 mg /kg/day, 8 h)

Amoxycillin is effective in treating infants due to beta-lactamase producing E-coli resistant to ampicillin. In uncomplicated acute cystitis with highly sensitive pathogens, single oral dose of 3 g is effective. May be repeated after 12 h. Alternatively 250 mg 8 h for 5 to 7 days. For children 125 mg 8 h.(20-40 mg/kg/day, 8 h)

Oral cephalosporins Cephalexin, cefadroxyl, cefuroxime, cefaclor can be used according to sensitivity patterns.

Prophylactic regime

1. Drink Sufficient water to void 2 L of urine/ day
2. Void 2-3 h with double micturition in patients with demonstrated vescico - ureteric reflux(VUR).
3. Void at bed-time and after sexual intercourse.
4. Avoid constipation which may impair bladder emptying.

Low dose antibacterial prophylaxis is indicated if there are 3 or more relapses or reinfection within 6 months and in complicated UTI. Drugs used are trimethoprim 100mg, co-trimoxazole 80/400mg, nitrofurantoin 50 to 100mg, nalidixic acid 250 mg, cephalexin 250 mg, norfloxacin 100 to 200 mg or ciprofloxacin 100 to 250 mg. These can be given as a single bed time dose. Prophylactic treatment should be continued for 12 months from the time of the last infection. Post coital treatment with a single dose antibacterial may be given to women with history of recurrent UTI precipitated by sexual intercourse.

10.3.2 Infections of the upper urinary tract

Acute pyelonephritis - severe renal infection may result in focal or multi focal infection in the kidney and may lead to abscess formation. Recurrent pyelonephritis often ensues urological abnormalities and results in scarring (chronic pyelonephritis). The acutely ill patients have to be hospitalised and require i.v. fluids, analgesics and immediate administration of antibiotics. Serum creatinine should be monitored.

Intravenous administration of ampicillin 1 g 6 h in combination with gentamicin 1.5 mg/kg as initial dose followed by 1 mg/kg 8 h is a good empirical combination before culture results are obtained. Intravenous cephalosporin may be administered as an alternative to ampicillin. Cefotaxime 1.5g 6 h or ceftazidime 2g 8 h are preferred. Intravenous fluoroquinolones such as ciprofloxacin 200 mg b.d. is equally effective. When fever and acute symptoms have been controlled for 24 h, patient may be switched over to oral treatment. In patients, who are not acutely ill, oral treatment may be started from the onset. In uncomplicated renal infection treatment should be continued for 2 weeks. A repeat culture after 10-14 days is essential. Relapse may require prolonged treatment for 6 weeks. In complicated infections prolonged treatment for 6 to 8 weeks is necessary followed by prophylaxis. If a patient fails to respond within 48 - 72 h of antibiotic therapy he should be referred to a centre with urological facilities.

10.4 PROSTATITIS

Common form of male UTI. Treated with 960 mg of Co-trimoxazole for 4 to 6 weeks or with trimethoprim 200 mg b.d. for similar duration. In patients resistant to trimethoprim, ciprofloxacin 500 mg b.d. for 4 to 6 weeks or ofloxacin 200 mg b.d. for similar duration can be used. In severely ill patients parenteral therapy with ampicillin (2 g) and gentamicin (3 to 5 mg/kg) may be given for 7 to 10 days.

10.5 CHRONIC BACTERIAL PROSTATITIS

Antibiotics shown to have high concentration in prostatic fluid include trimethoprim, fluoroquinolones, erythromycin, clindamycin and minocycline. Drug of choice is trimethoprim or co-trimoxazole. Treatment with co-trimoxazole (960 mg b.d.) or trimethoprim (200mg b.d.) should be continued for 6 weeks and may be required for longer period. This should be followed by long term, low-dose co-trimoxazole or trimethoprim for 6-12 months. The other drugs are used as per sensitivity patterns yielded by prostatic fluid culture.

10.6 CHRONIC RENAL FAILURE (CRF)

Syndrome resulting from progressive nephron loss. Symptoms start only when 75% of nephrons are damaged.

Recognition of 'Uremic Syndrome'

Unexplained weight loss, fatigue, lethargy, loss of appetite, anaemia, urinary symptoms like nocturia and polyuria are early symptoms.

Late symptoms include oedema, breathlessness, altered sleep, lack of concentration, vomiting, gastro intestinal bleed, mucosal and cutaneous ulcers and infections.

Common causes : chronic glomerulonephritis, diabetic nephropathy, hypertensive renal failure, reflux nephropathy, obstructive uropathies. Therapy is instituted when serum creatinine is $> 2 \text{ mg/dL}$ and /or creatinine clearance is $< 25 \text{ mL/min}$.

Treatment guidelines

Diet : Protein restriction - 0.6 g/kg/bw,

Salt 4 - 6 g/day.

Fluids 1.5 to 2.5 L depending on fluid status.

Potassium restriction - avoid citrus fruits, high protein diet and preserved food.

Caution: Blanket salt restriction and fixed recipes to be avoided. Changes required on and off. Some patient without oedema may require additional salt intake.

Treatment of hypertension

Phosphate Binders

Calcium carbonate 1 - 3 g/day in divided doses.

Calcium acetate 1 - 3 g/day in divided doses.

Aluminium hydroxide 2 - 4 g/day in divided doses. Not recommended for prolonged use due to potential aluminium toxicity.

Haematinics

If peripheral smear shows microcytic hypochromic anaemia, iron and folic acid supplements are required.

Alkali Therapy

1. Tablet : Sodium bicarbonate (300mg tablets) 1 to 3 g/day in divided doses.
2. Shohl's solution : 5-15 mL t.d.s. 1mL of shohl's solution contains 1 mEq/L of HCO_3 .
Because of its sodium content, caution in oedematous and severely hypertensive patients.

Vitamins D₃ supplements

Indicated to prevent renal osteodystrophy and to reduce the levels of circulating parathyroid hormone. Since 1 hydroxylation is done in the kidney hydroxylated derivatives such as alpha calcidol and calcitriol have to be prescribed in renal failure.

Drugs

1,25 dihydroxy cholecalciferol (calcitriol)

Dose: 0.25 mcg daily or alternate day, increased upto 1mcg daily if required.
1 a hydroxy cholecalciferol (alpha calcidol) 0.25 mcg -1mcg daily.

P/C: Serum calcium levels to be monitored every month initially and once in three months there after

Dose: 0.25-0.5 mcg/day

Erythropoietin

Specific for anaemia of chronic renal failure.

P/C : Ensure adequate iron stores. To be used only in specialist care.

Dose: 25 - 100 units/kg bw twice weekly as required. Parenteral iron supplements enhance efficacy.

10.7 RENAL CORTICAL ABSCESS (renal carbuncle)

This is the result of haematogenous infection, usually by *Staphylococcus aureus*. Intravenous vancomycin 1 g 12 h or i.v. flucloxacillin 1 g 6 h are the preferred antibiotics. Other antibiotics may be used according to bacterial sensitivity testing. Parenteral therapy should be continued for at least 7 days. Oral treatment should be continued for at least 4 weeks. If the abscess is more than 2 cm in size, it should be aspirated. Aspiration can be done under ultrasound guidance (USG) and computerised tomographic (CT) guidance.

10.8 INFECTED RENAL CYSTS

Treatment is by aspiration of pus and aggressive antibacterial therapy.

10.9 PERINEPHRIC ABSCESS

Causative organisms: *Staph aureus*, *E.coli*, *Proteus mirabilis*, or *Klebsiella* sp.

Treatment : Surgical drainage. Antibiotics should cover both normal uropathogenic bacteria and *Staph aureus*. Intravenous gentamicin (1mg/kg 8 h), combined with cefotaxime (1.5g 6 h) or ceftazidime (2g 8 h) i.v. are the preferred combinations. Therapy may be modified when results of bacterial sensitivity tests are available. Parenteral therapy should continue till the patient is afebrile for at least 24 h. Oral therapy should continue at least for 4 weeks.

10.10 URETHRAL SYNDROME

This is common in women of reproductive age group. Usually it is associated with low bacterial counts on culture. The treatment is appropriate with the antibacterial drug for 7 to 14 days. Culture negative urethral syndrome usually respond to tetracycline or doxycycline for 5 to 7 days.

11. HAEMATOLOGY

11.1 NUTRITIONAL ANAEMIA

1. As far as possible try to identify the deficiency by haemoglobin and blood smear examination.
2. Microcytic hypochromic anaemia occurring in Kerala is largely due to iron deficiency.
3. Macrocytic anaemia is mostly due to folate deficiency, either dietary or conditioned.
4. Management should consist of overall correction of diet plus supplementation by ferrous sulphate in case of iron deficiency anaemia and folate and B12 for macrocytic anaemia.
5. If response is unsatisfactory look for sources of bleeding and other causes.
6. 30 % of nutritional anaemia occurring in Kerala are due to combined deficiencies and therefore combination therapy with iron, folate and

- B₁₂ may be necessary. Compound preparations are available.
7. If the response is unsatisfactory (haemoglobin does not rise atleast 3 g within a month) refer for specialist help.
 8. Haemolytic anaemia, aplastic anaemia, leukemia, myeloma, lymphoma all should not be managed in institutions where haematological investigations are lacking.
In these conditions, in addition to ineffectiveness of empirical therapy many of them are worsened by such intervention.
 9. Severe anaemia - If the haemoglobin is below 4g/dL serious complications like cardiorespiratory failure may develop and so such patients may have to be referred to higher centres without delay.

11.2 HAEMORRHAGIC DISORDERS

1. Majority of them are due to local causes like injury to blood vessels or ineffective haemostasis.
2. Suspect underlying haemorrhagic disorders if they occur as -
 - a. repeated episodes of bleeding from unrelated sites and at different time frames.
 - b. positive family history.
 - c. unusually severe or prolonged bleeding from cuts and wounds.
 - d. Menorrhagia and exsanguination in girls at menarche and during periods.
3. Two-thirds of haemorrhagic episodes are due to platelet vascular disorders (purpuras) and one-third is due to coagulation defects.

In purpuric disorders, extravasated blood clots, whereas in coagulation defects extravasated blood remains fluid for much longer period. Bleeding time is prolonged in platelet vascular disorders and coagulation time is prolonged in coagulation defects. Many of these are manageable in centres with moderate facilities for investigations. The emergency may have to be tackled by the primary care physicians. Thereafter specialist help is necessary for diagnosis. Further the role of the primary health centre physician in such haemorrhagic disorders is to manage and follow up patients on day to day basis after obtaining specialists advice.

11.3 BLOOD AND BLOOD COMPONENT THERAPY

Transfusion medicine has reached a high level of technical advancement in modern times, transfusion of whole blood or blood components can be lifesaving, but if sufficient care is not taken during donor selection, collection, storage and administration of blood and blood components serious morbidity and even death may occur. As far as possible, except in an emergency only the specific blood component should be used for transfusion.

Blood

Replacement of whole blood : sudden loss of 30% of blood volume
(i.e) 1-1.5 L

Blood Component Therapy

Packed erythrocytes :	Anaemias
Platelet concentrates :	Thrombocytopenias and thrombocytopathies
Leucocyte concentrates :	These used to be given in agranulocytosis and drug induced neutropenias, but now these are seldom used. Reconstitution of the leucocytes is achieved by giving the colony stimulating factors GM-CSF and G-CSF.

Single donor plasma(SDP)

Fresh frozen plasma(FFP)

Blood products

Serum albumin	-	Hypoalbuminaemias
Fibrinogen	-	Fibrinogen deficiency (congenital or acquired)
Immunoglobulin	-a.	Congenital deficiency of immunoglobulins.
	b.	As immunomodulatory therapy in several immunemediated disease.
	eg.	immune thrombocytopenia, haemolytic anaemias,
		Guillain - Barre syndrome etc.
	c.	For passive transfer of immunity
	eg.	hepatitis A and B, rabies.
Coagulation factors :	Coagulopathies due to deficiency of one or more	
Factor VIII, IX		coagulation factors.
	eg.	haemophilia.

Prothrombin complex concentrate

Fresh frozen plasma

This is prepared by separating the plasma and freezing it at -80°C within six hours. It has to be stored at -20°C and at this temperature it is stable for one year. 1 unit is 200 - 250 mL. It contains all coagulation factors, especially factors V and VIII.

Indications

Bleeding due to multiple coagulopathies secondary to liver disease, disseminated intravascular coagulation (DIC) and bleeding due to massive blood transfusions.

Cryoprecipitate

Freezing plasma prepared from blood within 6 hours of collection at -80°C and then thawing to 4°C in a cryobath, membranous precipitate appears in the main bag after allowing the liquified plasma to transfer with a satellite bag. It contains factors VIII, vWF, fibrinogen, and fibronectin. Usual dose is 1 unit/10 kg bw.

Hazards of transfusion therapy

1. Volume overload, air embolism.
2. Febrile reactions.
3. Allergy to the blood or other components.

4. Microbial contamination of the product.
5. Toxicity of the anticoagulant and other chemicals used.
6. Metabolic complications.
7. Haemorrhagic reaction - especially after massive transfusion of stored blood.
8. Haemolytic reactions.
9. Immunological reactions.
10. Transfer of infection from donor to recipient.
11. Iron overload; each 250 mL of red cells introduces 250 mg of elemental iron into the recipient.

This iron gets accumulated in the bone marrow, liver, heart and pancreas and leads to haemosiderosis with parenchymal destruction. This complication is usually seen in persons who have received more than 100 transfusions. In order to avoid iron overload, iron chelating agents such as desferioxamine which is given as a s.c. infusion, or the oral drug deferiprone has also to be started early and continued indefinitely.

Storage requirements and shelf life of blood and blood products

	Storage requirements	Shelf life
Whole blood collected in citrate phosphate dextrose with adenine (CPDA) packed erythrocytes	2 - 6 °C	35 days
Frozen erythrocytes (reconstituted)	2 - 6 °C	24 hrs
Washed erythrocytes	2 - 6 °C	6 hrs
Granulocyte concentrates	room temperature	24 hrs
Platelet concentrates	22°C	5 days in specialised bags otherwise only one/day. Should be agitated constantly.
Fresh frozen plasma	- 40 °C to - 20 °C	12 months for labile factors
Cryoprecipitate	- 40 °C to - 20 °C	12 months

Autologous blood transfusion

In order to avoid the hazards of transfusion therapy, wherever elective surgical procedures are contemplated, the patient's blood can be collected 7-10 days before the procedure and stored for future use. Use of erythropoietin prior to withdrawal of blood helps to get greater yields.

Procedure to be followed in blood transfusion services

1. Proper hand washing before and after handling each patient.
2. Use of protective gloves by the attendants.
3. Use of face masks and eye-protectors when blood or body fluids are likely to splash.

Disinfection

Most of the disinfectants are capable of destroying almost all common microbes including HIV, if used properly. Since blood and tissue fluids will form protective coats over the organisms preventing their destruction by the chemicals the utensils have to be washed thoroughly and cleaned before applying the disinfectants.

The following disinfectants are amply effective when used in the recommended dosage.

1. Chlorine releasing compounds.
2. Iodine compounds - povidone iodine.
3. Ethyl alcohol - 70% - denatured spirit.
4. Cetrimide 1/1000 solution (savlon)
5. Dichloroxylenol 1.5% solution (dettol)

Blood and blood products should be given i.v. without delay once they are taken out of the refrigerated environment and reconstituted. At present all blood donors have to be screened for the following conditions.

Syphilis

Hepatitis B and C

HIV infection and malaria.

Blood transfusion has to be started using appropriate sized transfusion needle. Refrigerated blood should be brought to room temperature before being transfused. For the initial 10 min the blood should be given at the rate of 10 - 20 drops per minute, thereafter the rate is increased to 30 drops per minute for 30 min, after which the transfusion is given more rapidly, so as to complete the procedure within 90 - 120 minutes. The patient should be monitored for adverse reactions during the transfusion and for the next 48 h. The transfusion should be promptly stopped if reactions develop. All adverse reactions should be reported to the transfusion specialist, along with the unused blood specimen.

Table gives the indications for blood components and their abuse

	Indications	Abuse
Whole Blood	In life-threatening haemorrhage, surgery, postoperative states	For general well being as a substitute for medical therapy of anaemias.

Erythrocytes	To improve haemoglobin and oxygen carrying capacity in severely anaemic patients, super transfusion therapy in thalassemias	1. As a volume expander 2. To improve general well being and physical efficiency
Platelets	To control or prevent surgical or spontaneous bleeding associated with deficiencies of platelet number of function.	1. Routine management of thrombocytopenia.
Fresh frozen plasma	To replace clotting factors when specific deficiency is	As a simple volume demonstrable expander.

Procedure for emergency blood transfusion when the circumstances are not ideal

In all instances blood should be collected from donors only after proper screening tests for syphilis, hepatitis B and C, and HIV infection. Test kits are now available which detect all these disease within 30 minutes, in no instance should unscreened blood be given.

12. ENDOCRINOLOGY

12.1 DIABETES MELLITUS

In all cases of diabetes mellitus the diagnosis must be confirmed by atleast two abnormal blood sugar reports - fasting blood sugar above 140 mg% and or 2 h post prandial blood sugar above 200mg %. The management diabetes include dietary modification, regular exercise, drugs and patient education. All cases of type I diabetes (IDDM) must be treated with insulin only. The starting dose of insulin is usually 0.5 unit / kg bw daily of which two third intermediate acting insulin and one third short acting . insulin. Final insulin dose depends on the clinical response and the blood sugar values and may vary from person to person.

All type II diabetes (NIDDM), without much symptoms, can be tried on diet therapy and exercise for about 4 weeks before embarking on drug therapy. The drug selection depends upon the body weight and diabetic complications. Obese type II diabetes with normal renal and hepatic function can be started on metformin therapy initially. If there is no response sulfonyl urea (glybenclamide, glypizide) can be added to metformin. Normal weight or lean type II diabetes may be started on sulfonyl urea (glybenclamide, glypizide) for diabetic control initially. If after maximum dose of sulfonyl ureas and metformin the patient is still out of control, insulin therapy may be required. This insulin therapy can be started initially as a small bedtime dose of intermediate acting NPH insulin along with day time oral hypoglycemic drugs. This basal insulin therapy may be useful in some of the type II diabetic patients. If the patient is not been controlled by this he may have to go for twice daily insulin therapy.

The target of good control is a fasting blood sugar less than 120 mg %, a 2 h post prandial blood sugar of 160 mg % and a haemoglobin A1C of less than 6.5 %.

12.2 DIABETIC KETOACIDOSIS

When a diabetic patient presents with extreme weakness, abdominal pain, vomiting, tachypnoea and tachycardia, diabetic ketoacidosis has to be suspected. However this may be the first presentation of a diabetic state. This can be confirmed by demonstrating hyperglycemia of more than 300 %, and a positive urine or plasma ketone bodies.

On diagnosis all patients must be started on i.v. normal saline, 1st 500 mL in 2 hrs and then 500 mL 4 h, depending on the state of hydration. The i.v. fluid must be changed to glucose saline once the random blood sugar (RBS) comes below 250 mg% or urine sugar becomes less than 1%. All patients must be started on i.v. bolus of 10 units of regular insulin along with 10 units of i.m. insulin. Thereafter insulin must be continued 10 units i.m. hourly and dose adjusted as per blood sugar reports. Once the patient is having urinary output, 1 ampoule of potassium chloride 10 mL must be added to every bottle of i.v. fluids. For proper management frequent monitoring of blood sugar, electrolytes, blood urea and arterial blood gases are necessary and hence the patient may be referred to a higher centre.

12.3 HYPOGLYCEMIA

This is a very common medical emergency which demands prompt action. Suspect hypoglycemia in a diabetic on drug treatment who missed a meal or unable to take the food because of illness. Clinical features include anxiety, tremor, feeling of emptiness in the epigastrium, profuse sweating, cold extremities, raised blood pressure, exaggerated reflexes, convulsion and coma.

Treatment : If the patient is conscious give either 25 g glucose dissolved in 200 mL water orally. Alternatively sucrose 25 g in 200 mL of any drink, or any sweets if the patient is able to swallow. The condition improves within 10 min.

If the patient is drowsy or comatose give i.v. glucose 100 mL of 25 % solution rapidly within 2 min. Invariably the patient regains consciousness at the end of the injection. Once the patient is conscious give oral carbohydrates so that hypoglycemia may not recur. In children with hypoglycemia, where intravenous injection is difficult an i.m dose of 1 mg of glucagon will be helpful.

12.4 THYROID STORM

This condition is suspected when there is rapid deterioration of thyrotoxicosis with hyperpyrexia, severe tachycardia, high output cardiac failure and restlessness. This is usually precipitated by stress or infection or due to surgery in a case of thyrotoxicosis without proper preparation.

Emergency treatment include external cooling with tepid sponging and paracetamol 600 mg, starting an i.v. line with dextrose saline and giving an

initial dose of 100 mg. Hydrocortisone as a bolus. Oral medication consists of propranolol 80 mg stat, carbimazole 60 mg, and Lugol's iodine 8 drops. The patients may be transferred to a tertiary care where further treatment can be undertaken.

12.5 MYXOEDEMA COMA

This condition is suspected when a patient of hypothyroidism slips into hypothermia, hypotension, hypoventilation and coma. This is usually precipitated by sepsis, surgery, cold environment and sedatives. The core temperature measured by rectal temperature will be less than 35°C.

Emergency treatment includes rewarming the patients with blankets, giving i.v. hydrocortisone 100 mg and oral thyroxine 300 mcg and ventilatory support. Patient may be transferred to tertiary centre after giving the initial medication and supportive measures. The commonest cause of death in these condition is cardiac arrhythmia and hypoventilation.

12.6 ADRENAL CRISIS

This medical emergency is characterised by nausea, vomiting, dehydration, hyponatremia, hyperkalemia, weakness, lethargy and hypotension. It has to be suspected in any known Addisonian patient who gets any infection, illness or stressful state. The best strategy is to prevent it by detecting it early and prevent it by increasing the dose of corticosteroids.

The emergency management include starting an i.v. line with 5 % glucose saline and a bolus injection of 100 mg hydrocortisone. After this hydrocortisone may be given at doses of 100 mg 6 h or as a continuous infusion of hydrocortisone at the rate of 10 mg/h. Along with the other measures to correct the precipitating factors should be undertaken. Once the patient is stabilised and the precipitating factor treated, he may be put on his usual maintenance dose of oral corticosteroids.

12.7 HYPERCALCEMIA

Hypercalcemia may be the mode of presentation of severe primary hyperparathyroidism, extreme bone secondaries, paraneoplastic syndrome, hypervitaminosis D and sarcoidosis. Clinical features include dehydration, hypotension, abdominal pain, vomiting, fever and altered sensorium.

The emergency management include i.v. normal saline 3-4 L with i.v. furosemide (40 mg 8 h) till serum calcium falls to less than 10.5 mg/dL and correction of other electrolyte abnormalities. The other therapeutic measures to reduce serum calcium include salmon calcitonin 200 - 400 mg i.v. 8 h subcutaneously or mithramycin 25 mcg/kg i.v. or disodium phosphate i.v. 500 mL over 6 - 8 h. Corticosteroids at the dose of prednisolone 1 - 2 mg/kg may be useful in cases of hypercalcemia due to sarcoidosis. After initial hydration refer the patients to a higher centre for further evaluation.

13. OBSTETRICS & GYNAECOLOGY

13.1 HYPEREMESIS GRAVIDARUM

1. Confirm the diagnosis of pregnancy by clinical examination.
2. Exclude other causes for vomiting like, gastritis, jaundice and diabetic ketoacidosis.
3. Check urine for sugar and acetone.
4. After making a diagnosis of hyperemesis, start i.v fluids (5% or 10% dextrose, dextrose saline and Ringer lactate) until the dehydration is corrected.
5. If vomiting is not controlled antiemetics like promethazine (25 mg i.m) metoclopramide(10mg i.m.) can be given
6. Once patient tolerates oral feeds she must be advised to have sips of fluids first (ORS - Oral Rehydration Solution) preferred. Oral antiemetics like meclizine (2 tab h.s) or doxylamine succinate (2 tablets h.s.) may be continued.
7. Exclude vesicular mole by ultra sonography in all cases of hyperemesis.

13.2 ECTOPIC GESTATION

Ectopic pregnancy should be suspected

1. When patient presents with abdominal pain with missed periods, with or without bleeding P/V
2. When products are scanty in abortion evacuation or MR
3. Diagnosis:

a) Clinical examination :

Movement of cervix is painful, the size of the uterus is less than the period of amenorrhoea, adnexal tenderness or mass.

When ectopic pregnancy ruptures, the patient will be pale and in shock

b) Urine highly sensitive pregnancy test (like card test) is usually positive.

c) Ultra sound examination (trans vaginal) will help in excluding intra uterine pregnancy. When ectopic is suspected the patient should be transferred to a referral centre with facilities for surgery and blood transfusions.

In ruptured ectopic, patient should be transferred as early as possible to the referral centre, with i.v. line running.

13.3 ANTEPARTUM HAEMORRHAGE

Bleeding per vaginum after 28 completed weeks of gestation is called antepartum haemorrhage.

1. Start an i.v. line with a wide bore needle preferably a canula (18G)
2. Take blood for grouping, cross matching and clotting time.
3. Assess the general conditions of the patient - pulse, B.P., R.R., etc.
4. Give sedation injections pethidine 50-75 mg i.m. or morphine 5-7.5 mg i.m depending on the weight of the patient.

5. Depending on the degree of hypotension and anoxia, give nasal oxygen if available, keep the foot end of the bed elevated.
6. Put in an indwelling catheter to record the urine output.
7. Make a quick examination to form a provisional diagnosis regarding the causes of antepartum haemorrhage.
8. If placenta previa is suspected never do a vaginal examination to confirm.
9. Transfer the patient as quickly as possible to a centre where facilities for blood transfusions and caesarean section are available.
10. The relatives should be informed about the seriousness of the disease and the need for blood transfusion.

13.4 ECLAMPSIA

1. Take a quick history and do a quick examination to form a diagnosis. (Tonic clonic convulsions - high blood pressure and oedema).
2. Give anticonvulsants (any of the following).
 1. Diazepam 10 - 20 mg i.v.
 2. Phenytoin 400 mg i.v. - should be given very slowly watching the pulse and respiration.
3. Magnesium sulphate: 10 mL of 50% magnesium sulphate deep i.m. in each buttock (loading dose) using 20 G needle
Maintenance dose: 5 g every 4 h deep i.m. in the buttock.
Keep an i.v line running. Transfer the patient to a referral centre with facilities for anaesthesia and caesarean sections and intensive care facilities as quickly as possible.

13.5 PRETERM LABOUR

1. Confirm that the patient is in labour. (Regular intermittant and painful uterine contractions).
2. If pregnancy is less than 34 weeks, give tocolytics - drugs which inhibit uterine contractions.
 - a. Isoxsuprine hydrochloride 1 amp (100 mg) in 500mL 5% dextrose as i.v. drip. Start with 10-12 drops/min. Increase slowly until contractions are abolished. This can be continued for 24 hours. Then switch on to oral therapy with tablets of isoxsuprine Hcl.(10-20 mg t.d.s.)
 - b. Magnesium Sulphate 5 g i.m. 4-6 h can also be given until contractions are abolished. While the patient is on tocolytics carefully monitor the pulse rate, respiratory rate and blood pressure. Nifedipine 30 mg orally every hour is another drug that can be given. P.R., B.I.P., and R.R should be monitored carefully.
3. Give glucocorticoids i.m.
 - a. Betamethasone 12mg i.m 12 h 2 doses or
 - b. Dexamethasone 6 mg i.m 6 h and 4 doses may be given.Transfer the patient as quickly to a centre with good facilities for looking after preterm babies.

If patient cannot be monitored properly, tocolytics should not be given in the peripheral hospitals. Instead, after giving glucocorticoids, patient should be transferred to a tertiary care centre.

4. If pregnancy is more than 34 weeks the patient should be transferred to the nearest F.R.U (First Referral Unit). If the patient is in advanced labour, conduct the delivery. Keep the baby as warm and transfer immediately to a referral hospital.

13.6 PRE LABOUR RUPTURE OF MEMBRANES

1. Confirm diagnosis by giving a sterile pad, looking at the liquor or if needed by speculum examination.
2. Make sure whether the liquor is clear, mature blood-stained or meconium stained.
3. Give parenteral antibiotics combination of Inj.ampicillin 500 mg i.m. 6 h and Inj.gentamicin 80 mg i.m. 8 h is given. Metronidazole 500mg i.v. 8 h may be added if anaerobic infection is suspected or if prelabour rupture of membrane is for more than 24 hours.
4. If gestational period is 37 weeks or more, induction of labour can be done by giving oxytocin drip or PGE₂ gel.
2.5 to 5 units of oxytocins in 5% dextrose or normal saline.
PGE₂ gel is applied to the cervical canal under aseptic precautions. This may have to be supplemented with oxytocin.
5. If less than 37 weeks, give antibiotics and transfer to the referral centre where preterm babies can be looked after.

13.7 POSTPARTUM HAEMORRHAGE

1. Start i.v line with a wide bore canula (18G)
2. Take blood for grouping and cross matching and clotting time.
3. Start i.v. fluids for volume replacement (Normal saline, dextrose saline, blood volume expanders (polygeline), are the ones usually given).
4. Give sedation (Pethidine 50-75 mg i.m or morphine 5-7.5 mg) and oxygen. Keep the foot end raised if there is hypotension.
Differentiate between atonic and traumatic haemorrhage. If atonic, the uterus will be flabby.
Then give
 1. Oxytocin 10-20 units in normal saline as i.v drip.
 2. Ergometrine 0.2 mg i.v
 3. PGF₂ a 250 mcg i.m (if bleeding persists)

Traumatic postpartum haemorrhage is suspected when there is bleeding with a well contracted uterus. This should be suspected in instrumental deliveries . (vaccum extraction or forceps delivery). In traumatic postpartum haemorrhage, if there are no facilities for suturing and blood transfusions, a pressure pack should be kept in the vagina to arrest the bleeding temporarily.

After giving the first aid care, the patient should be transferred to a tertiary care centre with facilities for blood - transfusion, anaesthesia and surgical

intervention as quickly as possible. No time should be wasted. The patient should be transferred with i.v. fluid running.

It is desirable to have a hospital staff accompanying the patient.

13.8 HYPERTENSION IN PREGNANCY

Hypertension in pregnancy is classified as

- ♦ Pregnancy induced hypertension (toxemia)
 - preeclampsia
 - eclampsia
- ♦ Chronic hypertension - primary / secondary
- ♦ Chronic hypertension with super imposed toxemia
- ♦ Late gestational hypertension

Pregnancy induced hypertension is the most common cause of hypertensive complications in pregnancy. About 10% of all first pregnancies and 6% of all pregnancies is complicated by hypertension. Severe hypertension results in increased maternal and perinatal mortality.

Diagnosis

Blood pressure falls in pregnancy, reaches a nadir in mid trimester and thereafter rises. Supine blood pressure of 130/85 or a raise in BP of 20/10 mm Hg should be considered as hypertension, DBP of >110 mm Hg is defined as severe hypertension. Proteinuria of >300 mg per day is defined as preclampsia.

Treatment

Mild hypertension can be managed as out patient by non pharmacological measures, such as avoiding excess salt consumption and adequate sleep / rest for at least 8 hours a day (use tranquilisers if needed). Persistent DBP of >95 mm Hg should be managed by drug therapy.

Choice of drugs

1. Alphamethyl dopa - start with 125 mg b.d., can be increased upto 2 grams.
2. Calcium channel blockers - Nifedipine is commonly used.
Dose: 10-40 mg in divided doses. Delays labour and hence may have to be withdrawn in preterm
3. Beta adrenoreceptor blockers - Propranolol, atenolol and metoprolol are the commonly used drugs. Risk of foetal bradycardia and heart blocks when used in high doses at term.
4. Alpha adrenoreceptor blockers - Prazosin is used as second line drug.
Dose 0.5 to 4 mg daily in divided doses.
5. Clonidine - useful as second line drug.

Drugs to be avoided

ACE inhibitors are contraindicated - Teratogenic
Neuronal blockers and reserpine also to be avoided.

Diuretics are not used except in pulmonary oedema - risk of placenta ischemia, thiazides may be teratogenic.

Indications for termination

Maternal

1. Persistent severe hypertension DBP > 120 mm despite optimal drug therapy.
2. Oliguria, renal failure, cardiac failure.
3. Jaundice, low platelet count (HELLP syndrome), impending eclampsia.

Foetal

Foetal compromise, severe intrauterine growth restriction (IUGR).
Elective termination of pregnancy should be timed in such a way that both the maternal and foetal risks are minimized.

Indication for referral to higher centre

Persistent severe hypertension not responding to 2 or more drug combinations and IUGR are indicated for referral.

13.9 DIABETES IN PREGNANCY

Patient should have a pre pregnancy counselling. Oral hypoglycemic agents should be changed to insulin before attempting pregnancy and patient should be normoglycemic before she becomes pregnant.

Diabetic patient should be advised to have smaller, but frequent feeds (3 meals and 3 snacks). Glycemic state should be assessed weekly by blood sugar estimation (RBS and PPBS) and insulin dose adjusted. They should have an USG examination around 18 - 20 weeks of pregnancy for ruling out congenital anomalies. Well controlled diabetic patient can go to term. Foetal well being should be assessed frequently and timely intervention may be done if needed.

14. CANCER & PALLIATIVE MEDICINE

14.1 CANCER PAIN (WHO guidelines)

1. Cancer pain can, and should be treated.
2. Evaluation and treatment of cancer pain are best achieved by a team approach.
3. The first steps are to take a detailed history, and to examine the patient carefully, to determine if the pain is:
 - ♦ Caused by the cancer, related to the cancer, caused by anticancer treatment, or caused by an other disorder;
 - ♦ Part of a specific syndrome;
 - ♦ Nociceptive, neuropathic, or mixed nociceptive and neuropathic;
4. Treatment begins with an explanation and combines physical and

- psychological approaches, using both non-drug and drug treatments.
5. It is useful to have a sequence of specific aims, such as:
 - ♦ To increase the hours of pain-free sleep;
 - ♦ To relieve the pain when the patient is at rest;
 - ♦ To relieve pain when the patient is standing or active.
 6. Drugs alone usually give adequate relief from pain caused by cancer, provided that the right drug is administered in the right dose at the right time intervals.
 7. "By mouth": the oral route is the preferred route for analgesics, including morphine.
 8. "By the clock": for persistent pain, drugs should be taken at regular time intervals and not "as needed".
 9. "By the ladder"
 - ♦ Unless the patient is in severe pain, begin by prescribing a non-opioid drug and adjust the dose, if necessary, to the maximum recommended dose.
 - ♦ If or when the non-opioid no longer adequately relieves the pain, an opioid drug should be prescribed in addition to the non-opioid.
 - ♦ If or when an opioid for mild to moderate pain (e.g.. codeine) no longer adequately relieves the pain, it should be replaced by an opioid for moderate to severe pain (e.g. morphine).
 10. "For the individual": the right dose of an analgesic is the dose that relieves the pain. The dose of oral morphine may range from as little as 5 mg to more than 1000 mg.
 11. Adjuvant drugs should be prescribed as indicated.
 12. For neuropathic pain, a tricyclic antidepressant or an anticonvulsant is the analgesic of choice.
 13. "Attention to detail": it is essential to monitor the patient's response to the treatment to ensure that the patient obtains maximum benefit with as few adverse effects as possible.

15. EAR, NOSE & THROAT

15.1 EPISTAXIS

Epistaxis is bleeding from the nasal cavity, can be arterial or venous. Treatment consists of keeping nasal packs dipped in adrenaline solution. Other measures include cauterization and ligation of bleeding spot in intractable cases. Hypertension which is a common cause of epistaxis does not warrant any specific treatment except local measures, close monitoring, assurance and antihypertensive drugs. In selected cases sedatives may be required.

15.2 ACUTE LARYNGEAL OEDEMA DUE TO ALLERGIC ANGIOEDEMA

Patient presents with oedema of eyelids, lips or choking sensation. Ask for

any history of :

- Food allergy
- Drug allergy
- Insect bite
- Viral infections

Management :

- Keep the airway patent
- Parenteral steroids
- Adrenaline
- Antihistamines
- Oxygen inhalation

If persistent trecheostomy and intubation.

15.3 ACUTE TONSILLITIS

This is usually bacterial. The common organism is *Strep. haemolyticus*, *Strep. pneumoniae* and others. Antibiotics are given based on culture and sensitivity reports. Other symptomatic measures like analgesics and antipyretics are also given. Most of this respond to penicillin given as injection, procaine penicillin 4,00,000 – 6,00,000 units daily for 5 – 7 days. Oral penicillin phenoxymethyl penicillin in dose of 250-500 mg (4-8 lakh units 6 h at least 30 min before food). Children : 25-50 mg/kg/day 6-8 h for 8-10 days usually clears the infection. Alternative drugs include erythromycin, amoxycillin.

15.4 CHRONIC TONSILLITIS

Chronic tonsillitis may be the result of recurrent acute tonsillitis which is not properly treated or may be the result of acute infection persisting. The predisposing causes are enlarged tonsils and adenoids, naso respiratory allergy and such others. The infecting organisms are *S. hemolyticus*, *S. pneumonia* and others. Evaluation of infection should be attempted by identifying the organism and finding their drug sensitivity. In addition to drug therapy, if the condition is persistent, tonsillectomy and adenoidectomy may be required.

15.5 ACUTE SINUSITIS

This is a common condition which in most cases is of bacterial origin. The common causative organisms being *Strep. pneumoniae*, *H. influenza* and anaerobes.

Treatment includes antibiotics based on culture and sensitivity reports. Commonly used ones are amoxycillin, doxycycline and co-trimoxazole. In resistant cases, second generation cephalosporines or amoxycillin - clavulanic acid combination is used. Other symptomatic measures like decongestants, analgesics and antipyretics are also used. Steam inhalation with or without medication give symptomatic relief and hasten recovery.

15.6 CHRONIC SINUSITIS

This results from repeated attacks of acute sinusitis which is not fully

treated. Often there may be underlying predisposing factors such as deflected nasal septum or anatomical abnormalities of the turbinates and their meatus resulting in obstruction to drainage of the mucus. Nasorespiratory allergy precipitates infection and helps to perpetuate. Here in addition to medical measures as outlined above, surgical intervention like antral wash, endoscopic sinus surgery also may be required.

15.7 INFECTIONS OF THE EXTERNAL EAR

The causative organism in furunculosis of external ear is *Staphylococcus aureus* and hence the antibiotic of choice is ampicillin, cloxacillin or ampicillin-cloxacillin combination. the common organism responsible for diffuse otitis externa are *Staphylococcus aureus*, *B.proteus*, *E.coli*, and *Pseudomonas pyocyaneus* and more often the infection is mixed. Most of the infection may respond to ampicillin/ amoxicillin and cloxaillin combinations, but if no response then broad spectrum antibiotic has to be given.

15.8 INFECTION OF MIDDLE EAR

The usual causative organism for acute otitis media are *Streptococcus pneumoniae*, *Haemophilus influenzae*, *M.catarrhalis*, *Streptococcus pyogenes* and *staphylococcus aureus*. Ideally, antibiotics should not be prescribed without culture or gram stain. If an exudate is present, stains or cultures are easy to obtain and relatively reliable. When there is no visible exudate, an antibiotic can be selected on an empirical basis. Amoxicillin is the drug of choice and usually most patients respond to it. When resistant strains are encountered alternate drugs that are to be used are erythromycin, sulfisoxazole and trimethoprim-sulfamethoxazole combinations, clavulanic acid with amoxicillin, cephalexin, cefaclor and cefadroxil.

For acute otitis media, amoxycillin, cephadroxyl and cefaclor are the first line antibiotic. Trimethoprim-sulphamethoxazole is a good alternative. In chronic suppurative otitis media (CSOM) the microbial flora is a mixed one and therefore antibiotic combinations may be necessary. In CSOM with acute exacerbation, we should do a culture sensitivity of the pus from middle ear and appropriate antibiotics should be given. If the ear discharge does not clear after several days of therapy, the case should be referred for specialist consultation.

15.9 INFECTION OF NOSE AND PARANASAL SINUS

The causative organisms found in acute infections of nose and paranasal sinus are pneumococci, staphylococci, *M.catarrhalis*, *Bacillus pfieffer* and *B.friedlander*. Chronic infections the organisms are nearly always mixed.

Ideally antibiotics should be started after culture and sensitivity of a swab taken from nasal cavity. Considerable care must be taken to avoid contamination from nasal vestibule. To obtain a proper sinus specimen, it is necessary to perform a puncture of the antrum, sphenoid sinus or even the ethmoid sinus or pass a canula through frontal sinus if this is possible. An aspirating syringe is then used to inject normal saline solution and draw back a

sample of the sinus content. Amoxycillin, amoxycillin clavulanate or ampicillin-cloxacillin combination are ideal to treat acute sinusitis. If the sinusitis is secondary to a dental cause, metronidazole or tinidazole may also be needed to combat anaerobic infection.

Note: It is preferable to do antrum puncture in taluk or district hospital.

15.10 INFECTION OF OROPHARYNX

Ideally a culture and sensitivity of the throat should be done and appropriate antibiotics should be started. Most of the infections are caused by pneumococcus, Streptococcus viridans and Staphylococcus. Hence ampicillin or amoxicillin is the drug to be used first. In resistant cases broad spectrum antibiotics has to be used. Macrolides such as erythromycin and roxithromycin are effective alternatives to the penicillins.

15.11 PRINCIPLES IN THE CHOICE OF ANTIBIOTICS FOR ENT DISEASES

The selection of an antibiotic in any branch of medicine is based on a thorough knowledge of the usual causative organism responsible for the infection and the physician's experience. The effectiveness of the antibiotic, the cost factor, dosage convenience as well as patient's compliance all will count for the choice of the antibiotic.

16. OPHTHALMOLOGY

16.1 FOREIGN BODY IN THE EYE

On examination: Localized - congestion - bulbar or foreign body cornea

Treatment: Wash the eye with distilled water loaded in a 5 cc syringe (without needle) with upper eye lid everted. Start antibiotic drops. If foreign body does not dislodge refer to an ophthalmologist.

16.2 CONJUNCTIVITIS

On examination: Excessive discharge - matting of eye lashes - congestion +++ more in fornices

Treatment: frequent washing, use cotton swab to clean the lid. Antibiotic drops to be used hourly.

16.3 CHEMICAL BURN

Alkali burns are more dangerous than acid burns. Wash eye with normal saline or Ringer lactate solution. Connect the drip bottle to i.v. drip set and wash continuously with the upper eye lid everted. Apply antibiotic ointment.

16.4 IRIDOCYCLITIS OR UVEITIS

Complaints of pain and redness unilateral or bilateral

On examination: Congestion around corneal limbus

Hazy cornea, pupil irregular due to posterior synechiae

Treatment: Refer to ophthalmologist without delay to differentiate from angle closure attack. Treatment for iridocyclitis and angle closure glaucoma is entirely different and wrong treatment may give rise to adverse outcome. Therefore early referral to ophthalmologist is advisable.

16.5 RECOGNITION OF REFRACTIVE ERROR IN CHILD

History of child with clumsy handwriting, disinterestedness in studies, mistake in copying written matter from board, strong family history of short sight.

Treatment: Refer to an ophthalmologist.

16.6 IDENTIFICATION OF CATARACT FOR SURGERY

Mature cataract : white pupillary reflex, visual acuity-projection of light +

Immature cataract : grey reflex; surgery can be done in the visual acuity is below 6/12. Ideal to advise surgery with intra ocular lens implantation.

Pupillary reflex should be brisk to predict good prognosis in mature cataract

PART - III

**Suggested list of drugs
to be in stock at all the times
in the Government Hospitals
(Dispensary,
Primary Health Centre &
Taluk Hospitals)**

Sl. No.	Name of drug	Preparation & Specification	Quantity suggested		
			Disp.	PHC	Taluk
ANTI INFECTIVES					
Antimicrobial					
1.	Benzyl penicillin	inj 10 lac units	50	100	300
2.	Phenoxymethyl penicillin	tab 250mg	200	500	2000
3.	Procaine penicillin	inj 30 lac units	50	100	500
4.	Benzathine penicillin	inj 24 lac units	20	50	200
5.	Cloxacillin	cap 500mg	-	200	1000
6.	Ampicillin	inj 500mg	50	200	2000
7.	Amoxycillin	cap 250mg	100	500	5000
8.	Cephalexin	cap 500mg	-	-	1000
9.	Cephaloridine	inj 500mg	-	-	200
10.	Cefotaxime	inj 250mg	-	20	50
11.	Streptomycin	inj 1g	20	50	100
(exclusively for T.B patients)					
12.	Gentamicin	inj 40mg/mL	-	-	50
13.	Tetracycline	cap 250mg	100	300	1000
14.	Doxycycline	tab 100mg	-	200	500
15.	Erythromycin	tab 250mg	200	500	1000
16.	-do-	susp 125mg/5mL	50	200	1000
17.	Roxithromycin	tab 150mg	-	-	200
18.	Chloramphenicol	cap 250mg	200	200	500
19.	-do-	inj 1g vial	-	25	100
20.	-do-	applicap 1%	200	200	500
21.	-do-	eye drops 1%	25	100	300
22.	-do-	ear drops 5%	25	100	300
23.	Norfloxacin	tab 400mg	300	1000	3000
24.	Ciprofloxacin	tab 250mg	300	1000	3000
25.	-do-	200mL bottle	20	100	300
26.	Co-trimoxazole				
	(trimethoprim+ Sulphamethoxazole)	tab regular	250	1000	3000
27.	- do-	susp paediatric	200	1000	4000
28.	Silver sulphadiazine	cream 1% w/w	10	50	100
29.	- do-	drops 1% w/w	10	50	100
Antileprosy & anti T.B					
30.	Dapsone	tab 50mg	500	1500	2000
31.	Rifampicin	tab 400mg	200	1000	3000
32.	Isoniazid	tab 300mg	1000	3000	10000
33.	Pyrazinamide	tab 500mg	100	300	1000
34.	Ethambutol	tab 800mg	100	200	500
35.	Vancomycin	inj 0.5 g	-	-	30

36.	Clotrimazole	vaginal tab 100mg	100	300	1000
37.	-do-	powder 1% w/w	-	6	30
38.	-do-	lotion 1% w/w	-	30	50
39.	-do-	ear drops 1% w/v	20	50	100
Antiviral					
40.	Acyclovir	tab 200mg	-	-	15
Antimalarial					
41.	Chloroquine	tab 250mg	500	2000	5000
42.	Primaquine	tab 7.5 mg	50	200	500
43.	Quinine	tab 300mg	-	-	250
Antiprotozoal					
44.	Metronidazole	tab 400mg	300	1000	5000
45.	-do-	inj 500mg/mL	-	30	100
Local antiseptic					
46.	Povidone iodine	lotion 5%w/v	10	30	50
47.	-do-	oint 10 % w/v	10	30	50
Anthelmentic					
48.	Albendazole	tab 400mg	100	300	2000
49.	-do-	susp 200mg/5mL	50	200	2000
50.	Piperazine	syrup 750 mg/5mL	10	30	100
51.	Diethylcarbamazine citrate	tab 100mg	500	1000	3000
52.	Niclosamide	tab 500mg	25	100	200

GASTROENTEROLOGY

Antacids

53.	Aluminium hydroxide + Magnesium hydroxide/trisilicate	tab	1000	2000	5000
54.	Ranitidine	tab 150 mg	300	1000	5000
55.	Ranitidine	inj 20 mg/mL	20	100	300
56.	Omeprazole	tab 20 mg	-	-	200
57.	Dicyclomine	tab 20 mg	-	200	300

Antispasmodic

58.	Atropine sulphate	tab 600 mcg	150	300	500
59.	-do-	inj 0.6mg/mL	200	500	2000
60.	Propantheline bromide	tab 15 mg	-	-	300

Prokinetic

61.	Metoclopramide	inj 5 mg/mL	-	100	300
62.	Prochlorperazine	inj 12.5 mg/mL	20	100	300
63.	Promethazine	tab 25 mg	200	500	2000
64.	-do-	inj 25 mg/mL	50	200	500

Antidiarrhoeal

65.	Codeine phosphate	tab 15 mg	200	500	1000
66.	-do-	syrup 15 mg/5 mL	100	500	100

Laxative

67.	Bisacodyl	tab 5 mg	100	300	1000
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68.	Liquid paraffin			2 L	10 L	50 L
69.	Castor Oil			-	-	2 L
Adsorbent						
70.	Activated charcoal	tab		1000	3000	5000
Ulcerative colitis						
71.	Propatheline bromide	tab	15 mg	-	-	300
72.	Prednisolone	tab	5 mg	200	1000	3000
73.	Sulphasalazine	tab	500 mg	-	-	100
74.	Betamethasone	inj	4 mg/mL	50	200	1000
75.	Hydrocortisone	inj	100 mg vial	-	30	100
Vitamins & nutritional supplements						
76.	Vitamin A	caps	50,000 iu	10,000	30,000	1,00,000
77.	-do-	inj	50,000iu/amp	30,000	100	300
78.	Vitamin D (calciferol)- anti-rachitic vitamin	inj	3,00,000 iu/mL	-	-	30
79.	Vitamin K - coagulation vitamin	tab	0.66 mg	-	-	100
80.	-do-	inj	(amp)	-	-	100
81.	Vitamins B ₁ (thiamine, aneurin)	tab	10 mg	500	2000	5000
82.	-do-	inj	100 mg/mL	10	30	50
83.	Vitamin B ₂ (riboflavin)	tab	20 mg	1000	5000	10,000
84.	Vitamin B ₃ (nicotinic acid)	tab	100 mg	1000	5000	10,000
85.	Vitamin B ₆ (Pyridoxine)	tab	40 mg	100	500	1000
86.	Multi vitamins	tab		1000	10,000	50,000
87.	Vitamin B ₁₂ (cyanocobalamin)	inj	100 mcg/mL	30	100	500
88.	B ₁ , B ₆ , B ₁₂	inj		100	500	2000
89.	Folic acid	tab	5 mg	200	1000	5000
90.	Vitamin C	tab	100 mg	500	1000	5000
91.	Potassium citrate	bottle		50	200	500
Mineral supplements						
92.	Calcium lactate	tab	300 mg	5000	10,000	50,000
93.	Calcium gluconate	inj	100 mg/mL	50	200	500
94.	Magnesium sulfate	salt		1 kg	3kg	5 kg
95.	-do-	inj	2 mmol/mL	-	-	10amp
96.	Ferrous sulphate	tab	100 mg	10,000	30,000	1,00,000
97.	Ferrous sulphate + folic acid	tab		10,000	30,000	1,00,000
98.	Lugol's iodine			-	1 L	3 L
Intravenous solutions						
99.	Glucose 25 %	inj	25 mL (amp)	100	300	1000
100.	Glucose 50%	inj		25	100	200
101.	Normal saline with drip set			10	50	100
102.	Glucose saline with drip set			10	50	100
103.	Potassium chloride	inj	10 mL	-	20	50
104.	Sodium bicarbonate	inj	7.5 % (10 mL)	-	20	200
General drugs						
105.	Paracetamol	tab	500 mg	5000	25000	1,00,000

106.	-do-	inj	150 mg/mLamp	50	200	500
107.	Paracetamol paediatric drops		150 mg/mL (bottle)	100	500	2000
108.	Aspirin	tab	300 mg	1000	10,000	50,000

Sedatives

109.	Phenobarbitone	tab	60 mg	500	5000	10,000
110.	-do-	tab	30 mg	1000	10,000	25,000
111.	-do-	inj	200 mg/mL amp	20	100	200
112.	Diazepam	tab	5 mg	500	2000	10,000
113.	-do-	inj	5 mg/mL amp	50	500	1000

Antidotes to poison

114.	Atropine sulphate	inj	0.6 mg/mL	100	200	500
115.	Naloxone	inj	400mcg/mL amp	-	20	50
116.	Pralidoxime	inj	500 mg(vial)	-	-	50
117.	Ipecac syrup		bottle 50 mg	1	2	2
118.	Antisnake venom	inj		10 amp	25 amp	50 amp

CARDIOLOGY

119.	Lignocaine	inj	2 % (30 ml)	6	30	100
120.	Diphenyl Hydantoin (Phenytoin)	tab	100 mg	1000	3000	10,000
121.	-do-	inj	100 mg	10	30	100
122.	Digoxin	tab	0.25 mg	100	500	1000
123.	Dopamine hydrochloride	inj	200 mg/ 5 mL	-	-	20
124.	Isoprenaline (Isoproterenol)	tab	20 mg	-	100	200
125.	Adrenaline	inj	1/1000sol	30 amp	100 amp	300 amp

Antianginal

126.	Glyceryl Trinitrate	tab	0.5 mg	-	200	2000
127.	Intravenous nitroglycerine	amp	5 mg	-	-	50
128.	Streptokinase	inj	15,00,000 iu	-	-	3 vial
129.	Heparin	inj	5000 iu/mL	-	-	10
130.	Phenindione	tab	50 mg	-	-	500
131.	Pentazocine	inj	30 mg/mL	-	-	100
132.	Pethidine	inj	50 mg/mL	-	50	200

Antihypertensives

133.	Propranolol	tab	10 mg	300	1000	5000
134.	Atenolol	tab	50 mg	-	1000	5000
135.	Verapamil	tab	40 mg	-	500	1000
136.	Nifedipine	caps	10 mg	250	1000	3000

Diuretics

137.	Frusemide	tab	40 mg	300	1000	5000
138.	-do-	inj	20 mg/mL amp	50	250	5000
139.	Aminophiline	inj	250 mg/2mLamp	50	200	500
140.	Morphine sulphate	inj	1% vial	30	100	200
141.	Clonidine	tab	100 mcg	-	-	500

142.	Dextropropoxyphene	cap	65 mg	-	-	100
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RESPIRATORY DISEASES

143.	Ephedrine HCl nasal drops		0.75% w/v	100	-	-
144.	Xylometazoline nasal drops		0.1 % w/v	20	50	100
	(Antibiotics already included)					

Antihistamines

145.	Chlorpheniramine maleate	tab	4 mg	200	1000	5000
146.	Pheniramine maleate	inj	22.75 mg/mL	50	200	500
147.	Astemizole	tab	10mg	-	-	500

Antiasthmatics

148.	Ephedrine	tab	30 mg	1000	5000	10000
149.	Beclomethasone inhaler		100 mcg	-	-	100
150.	Oxygen inhalation cylinder			-	2	10
151.	Tincture benzoin			1 litre	3 litre	10 litre
152.	Salbutamol	tab	2, 4 mg	2000	20000	50000
153.	Salbutamol nebulizing solution		5mg/mL	-	-	50
154.	Theophylline	tab	200 mg	500	1000	10000
155.	Bromhexine	tab	8 mg	-	500	2000

ENDOCRINE DISORDERS

156.	Glibenclamide (Gliburide)	tab	5 mg	5000	20000	50000
157.	Metformin	tab	50 mg	5000	20000	50000
158.	Insulin human NPH plain 3070		40 iu/mL	10	50	100
159.	Insulin regular (plain)		40 iu/mL	10	50	200
160.	Hydrocortisone hemisuccinate	inj	100mg vial	-	50	200
161.	Prednisolone	tab	5 mg	200	1000	3000
162.	Thyroxin Sodium (T ₄)	tab	100 mcg	100	300	1000
163.	Carbimazole	tab	5 mg	-	300	1000
164.	Ethinyl oestradiol	inj	10 mg/mL	-	-	1000
165.	Medroxy Progesterone Acetate	tab	10 mg	-	-	500

NEUROLOGICAL DISORDERS

Anti epileptics

166.	Carbamazepine	tab	200 mg	-	-	1000
169.	Paraldehyde	inj	10 mL amp	-	-	50

Drugs for Head ache

170.	Paracetamol	tab	500 mg	5000	25000	1,00,000
171.	Dihydroergotamine	tab	1 mg	-	-	1000
172.	Propranalol	tab	10 mg	-	-	1000

Antidepressants

173.	Fluoxetine	tab	20 mg	200	1000	5000
174.	Flupenthixol Decanoate	tab	10 mg	200	1000	5000

Antiparkinsonian drug

175.	Benzhexol Hydrochloride	tab	2 mg	500	2000	5000
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Antipsychotic drugs

176.	Haloperidol	tab	0.25 mg	100	1000	3000
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177.	Triclofos Sodium	liq	500 mg/5 mL (bottle)	--100	300	
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Antimyasthenic

178.	Neostigmine	tab	15 mg	50	250	500
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179.	Neostigmine	inj	0.5 mg/mL	20	100	300
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MUSCULOSKELETAL DISORDERS

180.	Ibuprofen	tab	200 mg	500	5000	10,000
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181.	Diclofenac Sodium	tab	50 mg	—	1000	3000
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182.	Cortisone acetate (for intra articular)	inj	100 mg/mL	—	—	500
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HAEMATOLOGY

183.	Human anti-D immunoglobulin	inj	300 mcg	—	—	
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184.	Hydroxy Urea	tab	500 mg	—	—	1000
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185.	Cyclophosphamide	tab	50 mg	—	—	1000
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186.	Cyclophosphamide	inj	200 mg (vial)	—	—	2000
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187.	Pherindione	tab	50 mg	—	—	5000
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188.	Mannitol	inj	20% (200 mL)	—	—	2000
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ANAESTHETICS

189.	Thiopentone sodium	inj	1 g (vial)	—	—	500
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190.	Lignocaine	inj	2 % (vial)	10	50	200
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191.	Ethylchloride spray			15	50	200
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DERMATOLOGY

192.	Neomycin+bacitracin+polymixin	ointment		50	200	2000
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193.	Whitfield's Ointment			5 kg	20 kg	50 kg
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194.	Castellani's Paint			1 litre	5 litre	5 litre
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195.	Gentian Violet	solution		1 litre	5 litre	5 litre
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196.	Salicylic acid ointment	(5 - 20 %)		1 kg	5 kg	5 kg
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197.	Phenol			1 litre	5 litre	20 litre
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198.	Idoxuridine ointment	0.5 % w/w		—	—	
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199.	Acyclovir ointment	5 % w/w		—	—	
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200.	Liquid paraffin			1 litre	3 litre	5 litre
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201.	White soft paraffin			2 kg	5 kg	10 kg
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202.	Dithranol paste	1 % w/w		—	100	200
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203.	Potassium permanganate			500 g	1 kg	2 kg
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204.	Betamethasone skin ointment	0.05 % w/w		50	200	500
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205.	Betamethasone + neomycin ointment			50	200	500
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206.	Benzyl benzoate emulsion	25 % w / v	2 litre	5 litre	10 litre
207.	Gamma benzene hexachloride ointment	1 % w / w	1 kg	3 kg	3 kg
208.	Glycerine Magsulph		2 litre	10 litre	10 litre
209.	Povidone iodine ointment	5 % w / w	20	100	200
210.	Mercurous Chloride solution		2 litre	3 litre	3 litre

GYNAECOLOGY

211.	Oxytocin	inj 5iu/mL	–	–	20
212.	Nystatin vaginal pessaries	10,000 units	100	500	1000
213.	Povidone Iodine vaginal pessaries	200 mg	100	500	1000

ENT

214.	Beclomethasone nasal spray	50 mcg/dose	–	–	100
215.	Chloramphenicol ear drops	1 % w / v	20	50	100
216.	Norfloxacin ear drops	0.3 % w / v	20	50	100
217.	Sodium bicarbonate I.P.		2 kg	5 kg	10 kg
218.	Glycerol (for ear drops)		20	50	100
219.	Clotrimazole ear drops	1 % w / v	20	50	100

OPHTHALMOLOGY

Eye drops

220.	Penicillin G eye drops	10,000iu/mL	20	100	200
221.	Gentamicin eye drops	9.1 mg/mL	20	50	100
222.	Chloramphenicol applicaps	1 % w / w	100	500	1000
223.	Ciprofloxacin eye ointment	0.3 % w / w	20	50	100
224.	Ciprofloxacin eye drops	0.3 % w / v	20	50	100
225.	Xylocaine eye drops	4 % w / v	–	3	5
226.	Pilocarpine eye drops	0.5 % w / v	2	5	5
227.	Oral glycerine		–	2 litres	5 litres
228.	Hydrocortisone eye ointment	1.5 % w / w	10	30	50
229.	Homatropine eye drops	2 % w / v	5	10	20
230.	Fluorescein Sodium eye drops	2 % w / v	2	3	5

VACCINES & SERA

231.	Tetanus toxoid		50	100	300
232.	Antigangrene serum		–	–	10

Other vaccines and sera to be stored as per the directions of the Government from time to time based on vaccination strategies.

APPENDIX - I

SCHEDULE G DRUGS

1. Aminopterin
2. L-Asparaginase
3. Bleomycin
4. Busulphan; its salts
5. Carbutamide
6. Chlorambucil; its salts
7. Chlorothiazide and other derivatives of 1, 2, 4, benzothiadrazine
8. Chlorpropamide; its salts
9. Chlorthalidone and other derivatives of Chlorobenzene compound
10. Cis-platin
11. Cyclophosphamide; its salts
12. Cytarabine
13. Daunorubicin
14. Di-Isopropyl Eluorophosphate
15. Disodium Stilboestrol Diphosphate
16. Doxorubicin Hydrochloride
17. Ethacrynic acid; its salts
18. Ethosuximide
19. Glibenclamide
20. Hydantoin; its salt's, its derivatives, **their** salts
21. Hydroxy urea
22. Insulin, all types
23. Lomustine Hydrochloride
24. Mannomustine; its salts
25. Mercaptoprine; its salts
26. Metformin; its salts
27. Methsuximide
28. Mustine; its salts
29. Paramethadione
30. Phenacemide
31. Phenformin; its salts
32. 5-Phenylhydantoin; its alkyl and aryl derivatives; its salts
33. Primidone
34. Procarbazine Hydrochloride
35. Quinthalzone
36. Sarcolysine
37. Sodium 2-Mercaptoeth-anesul fonate
38. Tamoxiten citre
39. Testolactone
40. Thiotepa

41. Tolbutamide
42. Tretamine; its salts
43. Troxidone
44. Antihistaminic substances the following, their salts, their derivatives, salts of their derivatives
45. Antazoline
46. Bromodiphenhydramine
47. Buclizine
48. Chlorcyclizine
49. Chlorpheniramine
50. Clemizole
51. Cyproheptadine
52. Diphenhydramine
53. Diphenylpyraline
54. Doxylamine Succinate
55. Isothipendyl
56. Mebhydroline Napadisylate
57. Meclozine
58. Phenindamine
59. Pheniramine
60. Promethazine
61. Thenalidine
62. Triprolidine
63. Substances being tetra-N-substituted derivatives of ethylene Diamine or propylenediamine.

Note :- Preparations containing the above substances excluding those intended for topical or external use are also covered by this schedule.

APPENDIX - II

SCHEDULE H DRUGS

1. Adrenocorticotrophic hormone (ACTH)
2. Amloride Hydrochloride
3. Analgin
4. Androgenic Anabolic oestrogenic and progestational substances, the following:
Benzestrol
5. Derivatives of stilbene, dibenzyl or mepthalene with oestrogenic activity; their esters, steroid compounds with androgenic or oestrogenic or pregestational activity, their esters.
6. Allopurinol
7. Alphachymotrypsin
8. Amantidine Hydrochloride
9. Amitriptyline, its salts
10. Ammoidine
11. Ammodin
12. Antibiotics
13. Apiol
14. Aprotinin
15. Arsenic, organic compounds, of, for injection
16. Azathioprine
17. Barbituric acid, its salts, derivatives of barbituric acid, their salts, compounds of barbituric acid, its salts its derivatives, their salts with any other substance excluding those included in Sch. X.
18. Beclomethasone Dipropionate
19. Benactyzine, its salts
20. Betahistine Dyhydrochloride
21. Betamethasone 17 - Benzoate
22. Bethanidine Sulphate
23. Biperiden Hydrochloride
24. Bitoscanati
25. Bretylium Tosylate
26. Bromhexine hydrochloride
27. Bumetidine
28. Bupivacaine Hydrochloride
29. Carbenoxolone Sodium
30. Carbidopal
31. Carisoprodol
32. Cephaletin Sodium
33. Chloral Hydrate
34. Chlordiazepoxide; its salts

35. Chlorisondamine Chloride
36. Chlorpormazine, its salts
37. Chlorprothixene
38. Cimetidine
39. Citrated Calcium carbimide
40. Clindamycin
41. Clindinium Bromide
42. Clofazimine
43. Clofibrate
44. Clonidine Hydrochloride
45. Clopamide
46. Clotrimazole
47. Clorexolone
48. Corticosteroids, their esters, their derivatives and esters, or their derivative
49. Cyclandelate
50. Danazol
51. Dapsone, its salts and derivatives
52. Deoxyribonuclease
53. Diazepam
54. Diazoxide
55. Dilazep Hydrochloride
56. Dimethothazine Mesylate
57. Disopyramide
58. Disulfiram
59. Dopamine Hydrochloride
60. Dothiepin Hydrochloride
61. Doxapram Hydrochloride
62. Doxepin Hydrochloride
63. Drugs coming within the purview of the Dangerous Drugs Act
64. Econazole
65. Epinephrine; its salts
66. Epsilon Aminocaproic Acid
67. Ergot, alkaloids of, whether hydrogenated or not; their homologues any salts of any salts of any substances falling within this item.
68. Estradiol succinate
69. Ethacridine Lactate
70. Ethambutol Hydrochloride
71. Ethinyloestradiol
72. Ethionamide
73. Fenfluramine Hydrochloride
74. Flavoxate Hydrochloride
75. Flufenamic acid; its salts; its esters; their salts
76. Flupenthixol
77. Fluphenazine Enanthate and Decanoate

78. Flurbiprofen
79. Galanthamine Hydrobromide
80. Galliamine; its salts; its quaternary compound
81. Glucagon
82. Glycopyrolate
83. Glydiazinamide
84. Guanethidine
85. Halofuginone
86. Halogenated (Hydroxyquinoline) derivatives of Haloperidol
87. Heparin
88. Hyaluronidase
89. Hydroxyzine; its salts
90. Ibuprofen
91. Imipramine; its salts
92. Indapamide
93. Indomethacin; its salts
94. Intralipid Intravenous Fat Emulsion
95. Iron preparation for parenteral use
96. Isocarboxazid
97. Isonicotinic acid hydrazine and other hydrazine derivatives of isonicotinic acid; their derivatives, their salts.
98. Isosorbide Dinitrate
99. Isoxsuprine
100. Ketamine Hydrochloride
101. Ketoprofen
102. L-Dihydroxyphenylalanine
103. Levarterenol; its salts
104. Levodopa
105. Lidoflazine
106. Lithium Carbonate
107. Loperamide
108. Lorazepam
109. Mebendazole
110. Mebeverine Hydrochloride
111. Medigoxin
112. Mefenamic acid; its salts, its esters; their salts
113. Megestrol Acetate
114. Meglumine (Iocarmate)
115. Mephensesin; its esters
116. Mesterolone
117. Methicillin Sodium
118. Methixene; its salts
119. Methocarbamol
120. Methoxsalen
121. Methylpentynol; its esters and other derivatives

122. 1-methyl-4 Phenylpiperidine-4-carboxylic acid; esters of their salts
123. Metoclopramide
124. Metoprolol Tartrate Metrizamide
125. Metronidazole
126. Miconazole
127. Morphazinamide Hydrochloride
128. Nalidixic acid
129. Naproxen
130. Natamycin
131. Nicofuranose
132. Niflumic Acid
133. Nimorazole
134. Nitrazepam
135. Orphenadrine; its salts
136. Orazepam
137. Oxazolidine; its salts
138. Oxethazaine Hydrochloride
139. Oxolinic acid
140. Oxprenolol Hydrochloride
141. Oxyfedrine
142. Oxymetazoline
143. Oxyphenbutazone
144. Oxytocin
145. Para amino benzene sulphonamide, its salts, derivatives of para amino benzene sulphonamide having any of the hydrogen atoms of the para amino group of the sulphonamide group substituted by another radical excluding carbutamide; their salts.
146. Para amino salicylic acid; its salts; its derivatives; their salts
147. Pancuronium bromide
148. Pemidine; its salts
149. Penamcillin
150. Penicillamine
151. Pentazocine
152. Pentoxifylline
153. Phenelzine; its salts
154. Phenothiazine, derivatives of and salts of its derivatives not otherwise specified in the Schedule.
155. Phenylbutazone; its salts
156. Phenylpropanolamine Hydrochloride
157. Pimozide
158. Pindolol
159. Piracetam
160. Pivazide
161. Pituitary gland, the active principles of, not otherwise specified in

this Schedule and their salts.

162. Prednisolone stearoylglycolate
163. Promazine; its salts
164. Propanidid
165. Propranolol Hydrochloride
166. Pyrantel Pamoate
167. Pyrazinamide
168. Pyravinium; its salts
169. (Rauwolfia) alkaloids, their salts; derivatives of the alkaloids of rauwolfia; their salts.
170. Resoxacin
171. Salbutamol Sulphate
172. Saliovlazosulphapyridine
173. Sisomicin Sulphate
174. Sodium Cromoglycate
175. Sodium and Meglumine (Ilothalamates)
176. Sodium valporate
177. Sotalol
178. Spironolactone
179. Sulfonal; alkyl sulfonals
180. Sulphadexine
181. Sulphamethoxine
182. Sulphamethoxypyridazine
183. Sulphaphenazole
184. Sulthiame
185. Terbutaline Sulphate
186. Terizidone
187. Tetramisole Hydrochloride
188. Thiabendazole
189. Thiacetazone
190. Thiethylperazine
191. Thiopropazate; its salts
192. Thiothixene
193. Tinidazole
194. Tranylcypromine; its salts
195. Tretinoin
196. Tribromo-ethyl propanol
197. Trichloromethiazide
198. Trifluoperazine
199. Trifluoperiodol Hydrochloride
200. Trimeprazine, its salts
201. Trimetazidine Dihydrochloride
202. Trimethoprim
203. Tripropamine

204. Tylosin Tartrate
205. Urokinase
206. Vasopressin
207. Verapamil Hydrochloride
208. Xipamid

Note : Preparations containing the above substance excluding those intended for topical or external use are also covered by this schedule.

APPENDIX - III

SCHEDULE X DRUGS

1. Amobarbital
2. Amphetamine
3. Barbitol
4. Cyclobarbitol
5. Dexamphetamine
6. Ethchlorvynol
7. Glutethimide
8. Meprobamate
9. Methamphetamine
10. Methaqualone
11. Methylphenidate
12. Methylphenobarbital
13. Penobarbital
14. Phenacylidine
15. Phenmetrazine
16. Phenobarbital
17. Secobarbital

Note :

1. *Any stereoisometric form of the substance specified in this schedule, any salt of the substance and preparation containing such substances are also covered by this Schedule.*

2. *Preparations containing the above substances are also covered by this schedule :*

Provided, however, preparations containing Meprobamate or Phenobarbital in combination with other drugs may be exempted by the Licensing Authority from the provisions of this schedule, if satisfactory evidence is adduced that these preparations are not liable to be misused.

APPENDIX - IV

BANNED DRUGS

The manufacture and sale of the following drugs are prohibited by Government of India.

1. Amidopyrine
2. Fixed dose combinations of Vitamins with anti-inflammatory agents and transquillisers.
3. Fixed dose combinations of Atropine in Analgesics and Antipyretics.
4. Fixed dose combinations of Strychnine and Caffeine in tonics.
5. Fixed dose combinations of Yohimbine and Strychnine with Testosterone and Vitamins.
6. Fixed dose combinations of Iron with Strychnine, Arsenic and Yohimbine.
7. Fixed dose combinations of Sodium Bromide/Chloral hydrate with other drugs.
8. Phenecatin.
9. Fixed dose combinations of antihistaminics with antidiarrhoeals.
10. Fixed dose combinations of Penicillin with Sulphonamides.
11. Fixed dose combinations of Vitamins with Analgesics.
12. Fixed dose combinations of Tetracycline with Vitamin C.
13. Fixed dose combination of Hydroxyquinoline group of drugs with any other drug except for preparations meant for external use.
14. Fixed dose combinations of corticosteroids with any other drug for internal use.
15. Fixed dose combinations of Chloramphenicol with any other drug for internal use.
16. Fixed dose combinations of crude Ergot preparations except those containing Ergotamine, Caffeine, analgesics, antihistamines for the treatment of migraine, headaches.
17. Fixed dose combinations of Vitamins with anti-T.B. drugs except combination of Isoniazid with Pyridoxine Hydrochloride (Vitamin B-6).
18. Penicillin skin/eye ointment.
19. Tetracycline liquid oral preparations.
20. Nialamide.
21. Practolol.
22. Methapyrilene, its salts.
23. Methaqualone.
24. Oxytetracycline Liquid Oral preparations.
25. Demeclocycline Liquid Oral preparations.
26. Combination of Anabolic Steroids with other drugs.
27. Fixed dose combination of Oestrogens and Progestin (other than oral contraceptive) containing per tablet estrogen content of more than 50 mcg (equivalent to Ethinyl Estradiol) and of progestin

content of more than 3 mg (equivalent to Norethisterone Acetate) and all fixed dose combination injectable preparations containing synthetic oestrogen and progesterone.

28. Fixed dose combination of sedatives/hypnotics/anxiolytics with analgesic - antipyretics.
29. Fixed dose combination of Pyrazinamide with other anti-tubercular drugs except combination of Pyrazinamide with Rifampicin and INH as per recommended daily dose given below :-

<i>Drugs</i>	<i>Minimum</i>	<i>Maximum</i>
Rifampicin	450 mg	600 mg
INH	300 mg	400 mg
Pyrazinamide	1000 mg	1500 mg

30. Fixed dose combination of histamine H_2 - receptor antagonists with antacids except for those combinations approved by the Drugs Controller, India.
31. The patent and proprietary medicines of fixed dose combinations of essential oils with alcohol having percentage higher than 20% proof except preparations given in the Indian Pharmacopoeia.
32. All Pharmaceutical preparations containing Chloroform exceeding 0.5% w/w or v/v whichever is appropriate.
33. Fixed dose combination of Ethambutol with INH other than the following :
- | | |
|--------|------------|
| INH | Ethambutol |
| 200 mg | 600 mg |
| 300 mg | 800 mg |
34. Fixed dose combination containing more than one antihistamine.
35. Fixed dose combination of anthelmintic with cathartic/purgative except for piperazine.
36. Fixed dose combination of Salbutamol or any other bronchodilator with centrally acting anti-tussive and/or a antihistamine.
37. Fixed dose combination of laxatives and/or anti-spasmodic drugs in enzyme preparations.
38. Fixed dose combination of Metoclopramide with other drugs except for preparations containing metoclopramide and aspirin/paracetamol.
39. Fixed dose combination of centrally acting, anti-tussive with antihistamine having high atropine like activity in expectorants.
40. Preparations claiming to combat cough associated with asthma containing centrally acting anti-tussive and/or an antihistamine.
41. Liquid oral tonic preparations containing glycerophosphates and/or other phosphates and/or central nervous system stimulant and such preparations containing alcohol more than 20° proof.
42. Fixed dose combination containing Pectin and/or Kaolin with any drug which is systemically absorbed form GI tract except for combinations of Pectin and/or Kaolin with drugs not systematically absorbed.
43. Chioral Hydrate as a drug.
44. Dover's Powder I.P.

45. Dover's Powder Tables I.P.
46. Antidiarrhoeal formulations containing Kaolin or Pectin or Attapulgit or Activated Charcoal.
47. Antidiarrhoeal formulations containing Phthalyl Sulphathiazole or Sulphaguanidine or Succinyl Sulphathiazole.
48. Antidiarrhoeal formulations containing Neomycin or Streptomycin or Dihydrostreptomycin including their respective salts or esters.
49. Liquid Oral antidiarrhoeals or any other dosage form for paediatric use containing Diphenoxylate or Loperamide or Atropine or Belladonna including their salts or esters or metabolites, Hyoscyamine or their extracts or their alkaloids.
50. Liquid oral antidiarrhoeals or any other dosage form for paediatric use containing halogenated hydroxyquinolines.
51. Fixed dose combination of antidiarrhoeals with electrolytes.
52. Patent and Proprietary Oral Rehydration Salts other than those confirming to the following parameters
 - a. Patent and proprietary Oral Rehydration Salts on reconstitution to one litre shall contain :-
 - Sodium - 50 to 90 millimoles.
 - Total osmolarity - 240 -290 milli osmoles.
 - Dextrose : Sodium molar ration - Not less than 1:1 and not more than 3:1.
 - b. Patent and Proprietary cereal based Oral Rehydration Salts on reconstitution to one litre shall contain :-
 - Sodium - 50 to 90 millimoles.
 - Total osmolarity - not more than 290 milli osmoles.
 - Precooked rice - Equivalent to not less than 50 g and not more than 80 g as total replacement of Dextrose.
 - c. Patent and Proprietary Oral Rehydration Salts (ORS) may contain aminoacids in addition to Oral Rehydration Salt conforming to the parameters specified above and labelled with the indication for "Adult Cholera Diarrhoea only".
 - d. Patent and Proprietary Oral Rehydration Salts shall not contain Mono or Polysaccharides or saccharin sweetening agent.
53. Fixed dose combination of Oxyphenbutazone or Phenylbutazone with any other drugs.
54. Fixed dose combination of Analgin with any other drug other than antispasmodics.
55. Fixed dose combination of dextropropoxyphene with any other drug other than anti-spasmodics and/or non-steroidal anti-inflammatory drugs (NSAIDs).
56. Fixed dose combination of a drug, standards of which are prescribed in the Second Schedule to the said Act with an Ayurvedic, Siddha or Unani drug.
57. Fixed dose combination of Streptomycin with Penicillin.

APPENDIX - V

DENTAL PRACTITIONERS FORMULARY

1. Acyclovir cream
2. Acyclovir tablet
3. Alprazolam tablet
4. Amoxycillin capsule
5. Amoxycillin dispersible tablet
6. Amoxycillin dry syrup
7. Amoxycillin syrup
8. Ampicillin capsule
9. Ampicillin suspension
10. Aspirin tablet
11. Astemizole tablet
12. Azithromycin capsule
13. Benzydamine rinse
14. Betamethasone tablet
15. Carbamazepine syrup
16. Carbamazepine tablet
17. Carisoprodol tablet
18. Cephalexin capsule
19. Cephalexin syrup
20. Cephalexin tablet
21. Chlorhexidine gluconate 1 % gel
22. Chlorhexidine mouthwash
23. Chlorpheniramine tablet
24. Chlorzoxazone tablet
25. Choline salicylate dental gel
26. Ciprofloxacin tablet
27. Clindamycin capsules
28. Clindamycin suspension
29. Cloxacillin
30. Collossol iodine
31. Co-trimoxazole tablet
32. Cyclosporine capsule
33. Dextropropoxyphene
34. Diazepam syrup
35. Diazepam tablet
36. Diclofenac sodium 1% ointment
37. Diclofenac sodium tablet
38. Diphenhydramine capsule
39. Diphenhydramine syrup
40. Doxycycline capsule

41. Erythromycin ethyl succinate suspension
42. Erythromycin ethyl succinate tablet
43. Erythromycin stearate tablet
44. Fluconazole capsule
45. Fluconazole tablet
46. Gentamicin injection
47. Hydrocortisone cream
48. Hydrocortisone lozenges
49. Hydrogen peroxide mouthwash
50. Ibuprofen 5-10% gel
51. Ibuprofen suspension
52. Ibuprofen tablet
53. Indomethacin capsule
54. Ketoconazole tablet
55. Ketoprofen tablet
56. Ketorolac tablet
57. Lignocaine 2% injection
58. Lignocaine 5% ointment
59. Lignocaine with adrenaline 2% injection
60. Lincomycin capsule
61. Mefenamic acid
62. Metronidazole 1% gel
63. Metronidazole suspension
64. Metronidazole tablet
65. Miconazole 2% ointment
66. Multivitmain tablet
67. Nimesulide tablet
68. Nitrazepam tablet
69. Oxyphenbutazone tablet
70. Oxytetracycline capsule
71. Oxytetracycline tablet
72. Paracetamol suspension
73. Paracetamol tablet
74. Pentazocine injection
75. Phenoxymethyl penicillin tablet
76. Phenylbutazone
77. Piroxicam tablet
78. Povidone iodine solution 1%
79. Povidone iodine solution 5%
80. Prednisolone tablet
81. Promethazine syrup
82. Promethazine tablet
83. Protein supplement
84. Serratiopeptidase tablet

5. Sodium fusidate 2% ointment
6. Sodium perborate powder
7. Strontium chloride 10% gel
8. Tetracycline capsule
9. Tetracycline tablet
10. Tinidazole tablet
11. Triamcinolone dental paste
12. Triclosan 0.03% mouthwash
13. Vitamin A capsule
14. Vitamin A drops
15. Vitamin C tablet

APPENDIX - VI

NATIONAL ESSENTIAL DRUGS LIST

GOVERNMENT OF INDIA
MINISTRY OF HEALTH & FAMILY WELFARE, 1996

A

- Acenocoumarol
- Acetazolamide
- Acetyl Salicylic Acid
- Acriflavin + Glycerine
- Actinomycin D
- Activated charcoal
- Acyclovir
- Albendazole
- Albumin
- Allopurinol
- Aluminium hydroxide + Magnesium hydroxide
- Amikacin
- Aminophylline
- Amiodarone
- Amitriptyline
- Amlodipine
- Amoxicillin
- Amphotericin B
- Ampicillin
- Anti snake venom Serum
- Anti-D immunoglobulin (Human)
- Anti-Tetanus Human

- 23. Ascorbic acid
- 24. Atenolol
- 25. Atracurium
- 26. Atropine
- 27. Azathioprine

B

- 28. B.C.G vaccine
- 29. Barium sulfate
- 30. Beclomethasone
- 31. Benzathine benzylpenicillin
- 32. Benzoic acid + Salicylic acid
- 33. Benzoin compound
- 34. Benzyl Benzoate
- 35. Benzyl Penicillin
- 36. Betamethasone
- 37. Biperiden
- 38. Bisacodyl
- 39. Bleaching powder
- 40. Bleomycin
- 41. Bupivacaine
- 42. Busulfan

C

- 43. Calamine
- 44. Calcium Iodate
- 45. Calcium salts
- 46. Carbamazepine
- 47. Carbimazole
- 48. Centchroman
- 49. Cephalexin
- 50. Cetrimide
- 51. Chloramphenicol
- 52. Chlorhexidine
- 53. Chloroquine
- 54. Chlorpheniramine
- 55. Chlorpromazine
- 56. Chlorthalidone
- 57. Ciprofloxacin
- 58. Cisplatin
- 59. Clofazimine
- 60. Clomipramine
- 61. Cloxacillin
- 62. Co-trimoxazole (Trimethoprim + Sulphamethoxazole)
- 63. Coal tar
- 64. Codeine
- 65. Concentrated Vit. A Solution

- 66. Condoms with or without spermicide
- 67. Cyclophosphamide
- 68. Cyclosporin
- 69. Cytosine arabinoside

D

- 70. D.P.T Vaccine
- 71. Danazol
- 72. Dapsone
- 73. Desferoxamine
- 74. Dexamethasone
- 75. Dextran 70
- 76. Dextromethorphan
- 77. Diazepam
- 78. Diclofenac
- 79. Dicyclomine Hcl
- 80. Diethylcarbamazine
- 81. Digoxin
- 82. Dihydro Ergotamine
- 83. Diloxanide furoate
- 84. Diltazem
- 85. Dimercaprol
- 86. Diphtheria antitoxin
- 87. Dithranol
- 88. Dobutamine
- 89. Domperidone
- 90. Dopamine
- 91. Doxorubicin
- 92. Doxycycline

E

- 93. Enalapril
- 94. Epinephrine
- 95. Erythromycin
- 96. Ethambutol
- 97. Ether
- 98. Ethinylestradiol + Norgestrel
- 99. Ethinylestradiol + Levonorgestrel
- 100. Ethinylestradiol + Norethisterone
- 101. Ethinylestradiol
- 102. Ethyl chloride
- 103. Ethyl alcohol 70%
- 104. Etoposide

F

- 105. Factor IX complex (coagulation factors II, VII, IX, X)
- 106. Factor VIII concentrate
- 107. Ferrous salt

- 108. Fluorouracil
- 109. Fluorescein
- 110. Fluoxetine
- 111. Folic Acid
- 112. Folinic acid
- 113. Formaldehyde
- 114. Framycetin sulfate
- 115. Furosemide
- 116. Furazolidone

G

- 117. Gamma benzene hexachloride
- 118. Gentamicin
- 119. Gentian violet
- 120. Glibenclamide
- 121. Glucose with sodium chloride
- 122. Glucose
- 123. Glutaraldehyde
- 124. Glycerine IP
- 125. Glyceryl trinitrate
- 126. Griseofulvin

H

- 127. Haloperidol
- 128. Halothane
- 129. Heparin sodium
- 130. Hepatitis B vaccine
- 131. Homatropine
- 132. Hydrochlorothiazide
- 133. Hydrocortisone Sodium Succinate
- 134. Hydrocortisone
- 135. Hydrogen peroxide
- 136. Hyoscine N butylbromide

I

- 137. Ibuprofen
- 138. Imipramine
- 139. Immunoglobulin
- 140. Insulin injection (soluble)
- 141. Intermediate acting insulin (Lente / NPH insulin)
- 142. Intraperitoneal dialysis solution
- 143. Iopanoic acid
- 144. Iron dextran
- 145. Isoflurane
- 146. Isoniazid
- 147. Isoprenaline
- 148. Isosorbide - 5- mononitrate
- 149. Isoxsuprine

150. Isphagula
 151. IUD containing Copper
- K
152. Ketamine
 153. Ketoconazole
- L
154. L-Asparaginase
 155. Levodopa / carbidopa
 156. Levothyroxine
 157. Lignocaine
 158. Lithium Carbonate
 159. Local anaesthetic, astringent and anti inflammatory drugs.
 160. Loperamide
- M
161. Mannitol
 162. Measles vaccine
 163. Mebendazole
 164. Meglumine iothalamate
 165. Meglumine iotroxate
 166. Melphalan
 167. Mercaptopurine
 168. Metformin
 169. Methotrexate
 170. Methyl Ergometrine
 171. Methyldopa
 172. Methylprednisolone
 173. Methylrosanilinium
 174. Methylthioninium chloride (Methylene blue)
 175. Metoclopramide
 176. Metronidazole
 177. Mexiletine
 178. Miconazole
 179. Mitomycin - C
 180. Morphine
- N
181. Nalidixic acid
 182. Naloxone
 183. Neomycin + bacitracin
 184. Neomycin
 185. Neostigmine
 186. Niclosamide
 187. Nicotinamide
 188. Nifedipine
 189. Nitrofurantoin
 190. Nitrous oxide

- 191. Norethisterone
- 192. Norfloxacin
- 193. Normal Saline
- 194. Nystatin

O

- 195. Oral Polimyelitis vaccine (Live attenuated)
- 196. Oral rehydration salts
- 197. Oxygen
- 198. Oxytocin

P

- 199. Pancuronium
- 200. Paracetamol
- 201. Penicillamine
- 202. Pentamidine
- 203. Pentazocine
- 204. Pethidine
- 205. Pheniramine
- 206. Phenobarbital
- 207. Phenylephrine
- 208. Phenytoin Sodium
- 209. Pilocarpine
- 210. Polygeline
- 211. Polyvidone iodine
- 212. Potassium permanganate
- 213. Potassium iodide
- 214. Pralidoxime (2-PAM)
- 215. Praziquantel
- 216. Prednisolone
- 217. Primaquine
- 218. Procainamide
- 219. Procaine benzylpenicillin
- 220. Procarbazine
- 221. Prochlorperazine
- 222. Promethazine
- 223. Propranolol
- 224. Protamine sulfate
- 225. Pyrantel pamoate
- 226. Pyrazinamide
- 227. Pyridoxine

Q

- 228. Quinidine
- 229. Quinine

R

- 230. Rabies immunoglobulin
- 231. Rabies vaccine

- 232. Ranitidine
- 233. Retinol
- 234. Riboflavin
- 235. Rifampicin
- 236. Ringer lactate
- S
- 237. Salbutamol
- 238. Salicylic acid
- 239. Silver nitrate
- 240. Silver sulphadiazine
- 241. Sodium Stilboglucanate
- 242. Sodium Nitroprusside
- 243. Sodium + Meglumine diatrizoate
- 244. Sodium lothalamate
- 245. Sodium Thiosulfate
- 246. Sodium valproate
- 247. Sodium Nitrite
- 248. Spironolactone
- 249. Streptokinase
- 250. Streptomycin
- 251. Succinyl Choline
- 252. Sulfacetamide
- 253. Sulfadoxine + Pyrimethamine
- 254. Sulfasalazine
- T
- 255. Tamoxifen
- 256. Terbutaline
- 257. Testosterone propionate
- 258. Tetanus toxoid
- 259. Tetracaine
- 260. Tetracycline
- 261. Theophylline compounds
- 262. Thiamine
- 263. Thiopental Sodium
- 264. Timolol
- 265. Tinidazole
- 266. Trihexphenidyl
- 267. Tropicamide
- 268. Tuberculin, purified protein derivative
- U
- 269. Urokinase
- V
- 270. Verapamil
- 271. Vinblastine
- 272. Vincristine

- 273. Vit B12
- 274. Vit B-complex and multivitamins as per Sch. V
- 275. Vit D3 ergocalciferol
- 276. Vit. K
- W
- 277. Warfarin
- 278. Water for injection IP
- X
- 279. Xylometazoline

APPENDIX - VII

ESSENTIAL DRUGS LIST

Pregnancy Risk category

The pregnancy risk category identifies the potential risk to the foetus.

- A. Adequate studies in pregnant women have failed to show a risk to the fetus in the first trimester of pregnancy - and there is no evidence of risk in later trimesters.
- B. Animal studies have not shown an adverse effect on the foetus, but there are no adequate clinical studies in pregnant women.
- C. Animal studies have shown an adverse effect on the foetus, but there are no adequate studies in humans. The drug may be useful in pregnant women despite its potential risks.
- D. There is evidence of risk to the human foetus, but the potential benefits of use in pregnant women may be acceptable despite potential risks.
- X. Studies in animals or humans show foetal abnormalities or adverse reaction reports indicate evidence of foetal risk. The risks involved clearly outweigh potential benefits.

A

- 1. Acenocoumarol
- 2. Acetazolamide C
- 3. Acetyl Salicylic Acid D
- 4. Acriflavin + Glycerine
- 5. Actinomycin D
- 6. Activated charcoal

7. Acyclovir C
8. Albendazole
9. Albumin C
10. Allopurinol C
11. Aluminium hydroxide + Magnesium hydroxide C
12. Amikacin D
13. Aminophylline C
14. Amiodarone C
15. Amitriptyline D
16. Amlodipine
17. Amoxicillin B
18. Amphotericin-B B
19. Ampicillin B
20. Anti snake venom Serum
21. Anti-D immunoglobulin (Human)
22. Anti-Tetanus Human
23. Ascorbic acid A
24. Atenolol C
25. Atracurium C
26. Atropine C
27. Azathioprine D
B
28. B.C.G vaccine C
29. Barium sulfate
30. Beclomethasone C
31. Benzathine benzylpenicillin
32. Benzoic acid + Salicylic acid
33. Benzoin compound
34. Benzyl Benzoate
35. Benzyl Penicillin
36. Betamethasone C
37. Biperiden C
38. Bisacodyl C
39. Bleaching powder
40. Bleomycin D
41. Bupivacaine
42. Busulfan D
C
43. Calamine
44. Calcium Iodate
45. Calcium salts C
46. Carbamazepine C
47. Carbimazole
48. Centchroman B

49. Cephalexin
50. Cetrimide
51. Chloramphenicol C
52. Chlorhexidine
53. Chloroquine C
54. Chlorpheniramine B
55. Chlorpromazine C
56. Chlorthalidone B
57. Ciprofloxacin C
58. Cisplatin D
59. Clofazimine C
60. Clomipramine C
61. Cloxacillin B
62. Co-trimoxazole (Trimethoprim + Sulphamethoxazole) B (D at term)
63. Coal tar
64. Codeine
65. Concentrated Vit. A Solution
66. Condoms with or without spermicide
67. Cyclophosphamide D
68. Cyclosporin C
69. Cytosine arabinoside
D.
70. D.P.T Vaccine
71. Danazol X
72. Dapsone C
73. Desferoxamine
74. Dexamethasone C
75. Dextran 70 C
76. Dextromethorphan C
77. Diazepam D
78. Diclofenac B
79. Dicyclomine Hcl C
80. Diethylcarbamazine
81. Digoxin C
82. Dihydro Ergotamine X
83. Diloxanide furoate
84. Diltazem C
85. Dimercaprol C
86. Diphtheria antitoxin C
87. Dithranol
88. Dobutamine C
89. Domperidone
90. Dopamine C
91. Doxorubicin D
92. Doxycycline D

E

- 93. Enalapril C
- 94. Epinephrine C
- 95. Erythromycin C
- 96. Ethambutol B
- 97. Ether
- 98. Ethinylestradiol + Norgestrel
- 99. Ethinylestradiol + Levonorgestrel
- 100. Ethinylestradiol + Norethisterone
- 101. Ethinylestradiol X
- 102. Ethyl chloride
- 103. Ethyl alcohol 70%
- 104. Etoposide D

F

- 105. Factor IX complex (coagulation factors II, VII, IX, X) C
- 106. Factor VIII concentrate
- 107. Ferrous salt A
- 108. Fluorouracil D
- 109. Fluorescein C
- 110. Fluoxetine B
- 111. Folic Acid A
- 112. Folinic acid
- 113. Formaldehyde
- 114. Framycetin sulfate
- 115. Furosemide C
- 116. Furazolidone C

G

- 117. Gamma benzene hexachloride
- 118. Gentamicin C
- 119. Gentian violet C
- 120. Glibenclamide
- 121. Glucose with sodium chloride
- 122. Glucose
- 123. Glutaraldehyde
- 124. Glycerine IP C
- 125. Glyceryl trinitrate
- 126. Griseofulvin C

H

- 127. Haloperidol C
- 128. Halothane
- 129. Heparin sodium C
- 130. Hepatitis B vaccine B
- 131. Homatropine C
- 132. Hydrochlorothiazide B
- 133. Hydrocortisone Sodium Succinate C

- 134. Hydrocortisone C
- 135. Hydrogen peroxide
- 136. Hyoscine N butylbromide C

I

- 137. Ibuprofen B
- 138. Imipramine D
- 139. Immunoglobulin B
- 140. Insulin injection (soluble) B
- 141. Intermediate acting insulin (Lente / NPH insulin) B
- 142. Intraperitoneal dialysis solution
- 143. Iopanoic acid
- 144. Iron dextran C
- 145. Isoflurane
- 146. Isoniazid C
- 147. Isoprenaline C
- 148. Isosorbide - 5- mononitrate C
- 149. Isoxsuprine C
- 150. Isphagula
- 151. IUD containing Copper

K

- 152. Ketamine D
- 153. Ketoconazole C

L

- 154. L-Asparaginase C
- 155. Levodopa / carbidopa C
- 156. Levothyroxine A
- 157. Lignocaine B
- 158. Lithium Carbonate D
- 159. Local anaesthetic, astringent and anti inflammatory drugs.
- 160. Loperamide* B

M

- 161. Mannitol C
- 162. Measles vaccine X
- 163. Mebendazole C
- 164. Meglumine iofthalamate
- 165. Meglumine iotroxate
- 166. Melphalan D
- 167. Mercaptopurine D
- 168. Metformin
- 169. Methotrexate D
- 170. Methyl Ergometrine
- 171. Methyldopa C
- 172. Methylprednisolone C
- 173. Methylrosanilinium
- 174. Methylthioninium chloride (Methylene blue) C

- 175. Metoclopramide B
- 176. Metronidazole B
- 177. Mexiletine C
- 178. Miconazole B
- 179. Mitomycin - C C
- 180. Morphine C

N

- 181. Nalidixic acid B
- 182. Naloxone B
- 183. Neomycin + bacitracin
- 184. Neomycin C
- 185. Neostigmine C
- 186. Niclosamide B
- 187. Nicotinamide
- 188. Nifedipine C
- 189. Nitrofurantoin B
- 190. Nitrous oxide
- 191. Norethisterone X
- 192. Norfloxacin C
- 193. Normal Saline
- 194. Nystatin B

O

- 195. Oral Polio myelitis vaccine (Live attenuated) C
- 196. Oral rehydration salts
- 197. Oxygen
- 198. Oxytocin

P

- 199. Pancuronium C
- 200. Paracetamol
- 201. Penicillamine
- 202. Pentamidine C
- 203. Pentazocine C
- 204. Pethidine
- 205. Pheniramine
- 206. Phenobarbital D
- 207. Phenylephrine C
- 208. Phenytoin Sodium D
- 209. Pilocarpine C
- 210. Polygeline
- 211. Polyvidone iodine
- 212. Potassium permanganate
- 213. Potassium iodide D
- 214. Pralidoxime (2-PAM) C
- 215. Praziquantel B
- 216. Prednisolone C

- 217. Primaquine C
- 218. Procainamide C
- 219. Procaine benzylpenicillin
- 220. Procarbazine D
- 221. Prochlorperazine C
- 222. Promethazine C
- 223. Propranolol C
- 224. Protamine sulfate C
- 225. Pyrantel pamoate C
- 226. Pyrazinamide C
- 227. Pyridoxine A

Q

- 228. Quinidine C
- 229. Quinine X

R

- 230. Rabies immunoglobulin B
- 231. Rabies vaccine C
- 232. Ranitidine B
- 233. Retinol A
- 234. Riboflavin A
- 235. Rifampicin C
- 236. Ringer lactate C

S

- 237. Salbutamol
- 238. Salicylic acid C
- 239. Silver nitrate C (1%)
- 240. Silver sulphadiazine B
- 241. Sodium Stilboglucuronate
- 242. Sodium Nitroprusside C
- 243. Sodium + Meglumine diatrizoate
- 244. Sodium lothalamate
- 245. Sodium Thiosulfate
- 246. Sodium valproate D
- 247. Sodium Nitrite
- 248. Spironolactone C
- 249. Streptokinase C
- 250. Streptomycin D
- 251. Succinyl Choline C
- 252. Sulfacetamide C
- 253. Sulfadoxine + Pyrimethamine C
- 254. Sulfasalazine B (Dat term)

T

- 255. Tamoxifen D
- 256. Terbutaline B
- 257. Testosterone propionate X

- 258. Tetanus toxoid C
- 259. Tetracaine
- 260. Tetracycline D
- 261. Theophylline compounds C
- 262. Thiamine A
- 263. Thiopental Sodium C
- 264. Timolol C
- 265. Tinidazole
- 266. Trihexphynidyl C
- 267. Tropicamide
- 268. Tuberculin, purified protein derivative C
- U
- 269. Urokinase B
- V
- 270. Verapamil C
- 271. Vinblastine D
- 272. Vincristine D
- 273. Vit B12 A
- 274. Vit B-complex and multivitamins as per Sch. V
- 275. Vit D3 ergocalciferol C
- 276. Vit. K C (X if used in third trimester or near term)
- W
- 277. Warfarin D
- 278. Water for injection IP
- X
- 279. Xylometazoline C

INDEX

- Acarbose 193
- ACE Inhibitors 347
- Aceclidine 434
- Acenocoumarol 139
- Acetaminophen 226
- Acetazolamide 182, 288, 336, 436
- Acetyl cystine 184
- Acetyl salicylic acid 225
- ACTH – Adrenocorticotrophin 201
- Activated charcoal 91
- Acyclovir 48, 49, 72, 346, 370, 371, 376, 433
- Adenine arabinoside (vidarabine) 433
- Adenosine arabinoside 370
- Adrenal Hormones 213
- Adrenaline 393
- Adrenochrome 187
- Agar 89
- Alandronate Sodium 212
- Albendazole 64, 68, 387
- Alkylating Agents 407
- All Trans Retinoic Acid (ATRA) 419
- Allopurinol 59, 60, 249, 250, 341
- Almitrine bimesylate 181
- Alpha Methyldopa 153
- 5- Alpha reductase inhibitor 343
- Alpha tocopherol 108
- Alprazolam 320
- Altepase 277
- Aluminium acetate 381
- Aluminium chloride hexahydrate 381
- Aluminium hydroxide 73
- Amantadine 49, 51, 294, 327
- Ambroxol Hydrochloride 184
- Amethocaine 359
- Amikacin 19, 69, 385
- Amiloride 144, 336
- Amino acids with minerals and multi vitamins 120
- Aminoglycosides 17, 164, 345
- Aminophylline 174, 393
- Amiodarone 126, 439
- Amithizone 41
- Amitriptyline 313, 344
- Amlodipine 150

Ammonium chloride 183
 Amodiaquine 53
 Amoxapine 314
 Amoxycillin 11, 69, 71, 363, 383
 Amphotericin - B 42, 59, 60, 72, 346, 365, 369, 433
 Ampicillin 11, 69, 70, 71, 383
 Amrinone 129
 Anabolic steroids 223
 Androgens 418
 Aneurin 109
 Antacids 73
 Anterior Pituitary Hormones 201
 Anthelmintics 64
 Anti acne lotion 377
 Anti oestrogens 198
 Antiandrogens 222
 Anticancer drugs 439
 Anticholinesterases 278
 Anticoagulants 188, 271
 Antidepressants 439
 Antifungal drugs 42
 Antigens for immunotherapy 179
 Antihistamines 377
 Antimalarial drugs 53
 Antimonials 59
 Antiparasitic agents 53
 Antiparkinsonism drugs 439
 Antiprotozoal drugs 53
 Antispasmodic 79
 Antithyroid drugs 206
 Antiviral drugs 48
 Aprotinin 276
 Artemether 53, 56
 Artemisinin 58
 Artesunate 53
 Artificial nutritional support 121
 Ascorbic acid 114, 344
 Aspirin 136, 225, 238, 271, 390
 Astemizole 162, 392, 426
 Atenolol 147, 397
 Atracurium Besylate 356
 Atropine sulphate 80, 354, 391, 437
 Auranofin 244
 Aurothioglucose 244
 Azatadine Maleate 426
 Azathioprine 94, 246, 253, 268, 339, 376

Azelastine hydrochloride 159
Azithromycin 26, 364, 386
AZT + Dideoxycytosine 72
Bacitracin 28, 361, 432
Baclofen 280
Beclomethasone Dipropionate 161, 176, 394, 422
Bendrofluazide 332
Benzathine penicillin 7
Benzhexol Hydrochloride 296
Benzocaine 359
Benzonatate 183
Benzoyl peroxide 377
Benztropine 327
Benzydamine hydrochloride 424
Benzyl benzoate 379
Benzyl penicillin 7
Beta blockers 144, 126, 235
Betahistine Dihydrochloride 304
Betamethasone 214, 252, 423, 436
Betaxolol 435
Bethanechol 343
Bezafibrate 141
Biguanides 192
Biotin 112
Biperiden 297, 327
Bisacodyl 88
Bismuth compounds 78
Bisoprolol 147
Bisphosphonate 212
Bleomycin 415
Bretylium 127
Broad spectrum penicillin 71
Bromhexine 184
Bromocriptine 295
Budesonide 162, 177, 394, 422
Bumetanide 143, 334
Bupivacaine 358
Buprenorphine hydrochloride 229
Buserelin 200
Buspirone Hydrochloride 322
Busulphan 260, 409
Calamine 381
Calciferol 106
Calcitonin 209
Calcitriol 212, 372
Calcium and its Salts 210

Calcium carbonate 73, 117
 Calcium channel blockers 127, 148, 235, 319
 Calcium chloride 117
 Calcium gluconate 117
 Calcium lactate 117
 Calcium 117
 Calipotriol 373
 Cantharidin 370
 Capreomycin 169
 Captopril 156, 342, 397
 Carbachol 343
 Carbamazepine 233, 282, 319, 395
 Carbenicillin 12, 432
 Carbimazole 207
 Carbochol 434
 Carbohydrates 102
 Carboplatin 420
 Carisoprodol 281
 Carvedilol 48
 Castellani's Paint 368
 Castor Oil 90
 Cefaclor 14, 15, 384
 Cefadroxil 13, 15, 384
 Cefazolin 15, 384
 Cefepime 14, 17
 Cefixime 14, 16, 384
 Cefoperazone 14, 16
 Cefotaxime 14, 17, 69, 70, 384
 Cefotetan 14, 16
 Cefoxitin 14, 16
 Ceftazidime 14, 16, 71, 384
 Ceftizoxime 14, 16
 Ceftriaxone 14, 17, 69, 70, 71
 Cefuroxime 14, 16, 69, 71
 Cephalexin 13, 15, 383
 Cephaloridine 13, 15
 Cephalosporins 13 - 17, 69, 71, 164, 346, 363, 383
 Cephalothin 13, 15
 Cephazolin 13, 15, 432
 Ceruminolytics 424
 Cetirizine 163, 392, 425
 Chelated iron 119
 Chenodeoxycholic acid 95
 Chloral Hydrate 323
 Chlorambucil 263, 338, 408
 Chloramphenicol 27, 69, 70, 71, 385, 423, 432

Chlordiazepoxide 321
 Chlorhexidine 424
 Chloroquine 53, 57, 59, 61, 245, 388
 Chlorpheniramine Maleate 425
 Chlorprocaine 359
 Chlorpromazine 300, 305
 Chlorpropamide 191
 Chlortetracycline 22
 Chlorthalidone 142, 331
 Chlorxylenol 425
 Cholecalciferol 211
 Cholestyramine 342
 Choline salicylate 424
 Chrysotherapy 376
 Ciclopirox 365
 Ciclopiroxolamine 42
 Cimetidine 74
 Cinnarizine 298
 Ciprofloxacin 30, 71, 94, 364, 387, 423, 432
 Ciprofloxacin+broad spectrum penicillin 71
 Cisapride 82, 92, 391
 Cisplantin 347, 420
 Clarithromycin 25, 79, 365
 Clemastine 427
 Clidinium 82
 Clindamycin 34, 69, 70, 71, 362, 377
 Clofazamine 41
 Clomiphene Citrate 199, 406
 Clomipramine Hydrochloride 314
 Clonazepam 288
 Clonidine 153, 327
 Clotrimazole 42, 45, 64, 72, 368, 424, 425, 433
 Cloxacillin 10, 69, 385
 Clozapine 311
 Coal Tar Ointment 372
 Co-careldopa (Carbidopa + Levodopa) 294
 Cocaine 438
 Codeine Phosphate 85, 182, 230
 Colchicine 249, 376
 Colistin 29
 Conjugated oestrogen 218
 Corticosteroids 93, 242, 263, 266, 420
 Cortisone 213, 436
 Co-trimoxazole 38, 70, 164, 386
 Crotonamiton 380
 Cyanocobalamin 112

Cyclizine 299
 Cyclopentolate 437
 Cyclophosphamide 248, 253, 268, 338, 376, 407
 Cycloserine 170
 Cyclosporin 247, 256, 339, 374, 379
 Cyproheptadine 392, 427
 Cyproteron Acetate 222
 Cytarabine (cytosine arabinoside) 413
 Dacarbazine 381, 409
 Dalteparine sodium 138
 Danazol 268, 376
 Dapsone 40, 375, 376
 Daunorubicin 415
 Deferiprone 260
 Demecarium bromide 434
 Deoxy corticosterone acetate 214
 Dequalinium chloride 425
 Desferrioxamine 259
 Desmopressin 204, 344,
 Dexamethasone 214, 243, 252, 437
 Dextroamphetamine 328
 Dextromethorphan 183
 Dextropropoxyphene Hydrochloride 230
 Diamidines 59
 Diazepam 280, 319, 395, 396
 Diazoxide 151
 Diclofenac Sodium 239
 Dicyclomine 79, 391
 Diethylcarbamazine 66, 68, 388
 Digestive enzymes 92
 Digoxin 128, 397, 439
 Dihydrocodeine 182
 Dihydroergotamine 234
 Dihydrotachysterol 211
 1,25 dihydroxy Cholecalciferol (Calcitriol) 212
 Dilantin Sodium 395
 Diloxanide furoate 61, 389
 Diltiazem 149, 319
 Dimenhydrinate 299
 Dimethindene maleate 427
 Dimethyl Sulfoxide (DMSO) 370
 Dinitrochlorobenzene (DNCB) 378
 Dioctyl Sodium Sulfosuccinate 91
 Diphenhydramine 392, 428
 Diphenoxylate 86
 Diphenyl hydantoin 125

Dipyridamole 124, 136, 271
 Distigmine 343
 Disulfiram 326
 Dithranol 372, 378
 Diuretics 142
 Dobutamine 131, 523
 Docusate sodium 91, 424
 Domperidone 81, 92, 301, 392
 Dopamine hydrochloride 130, 398, 523
 Dothiepin Hydrochloride 315
 Doxapram 181
 Doxepin Hydrochloride 315
 Doxorubicin 414
 Doxycycline 23, 58, 59, 69, 71
 Dyhydrogesterone 220
 Echothiophate iodide 434
 Econazole 365, 434
 Edrophonium Chloride 279
 Embramine 428
 Emollients 371
 Enalapril 156, 397
 Enflurane 353
 Enoxaparine 138
 Ephedrine 160
 Ephedrine hydrochloride 421
 Epinephrine 435, 438
 Epsilon amino caproic acid (EACA) 275, 376
 Ergocalciferol 211
 Ergotamine tartrate 233
 Erythromycin 23, 69, 70, 363, 377, 385
 Erythropoietin 257
 Esmolol 147
 Essential amino acid with multivitamins 120
 Ethacrynic acid 143, 334
 Ethambutol 167, 389
 Ethinyl oestradiol 218, 417
 Ethionamide 42, 170
 Ethosuximide 283
 Ethyl alcohol 439
 Ethyl oestrenol 218, 219
 Etomidate 351
 Etoposide 420
 Exfoliants 377
 Exosurf 185
 Famciclovir 48
 Famotidine 75

Fats 104
 Felodipine 150
 Female sex hormones 216
 Fentanyl Citrate 230
 Ferrous fumarate 119
 Ferrous gluconate 119
 Ferrous succinate 119
 Ferrous sulphate (hydrated) 119
 Fexofenadine 163, 428
 Finasteride 223
 Fissure in ano 93
 Flavoxate 343
 5 - fluorouracil 370, 38, 412
 Fluconazole 42, 47, 72, 369
 Flucytocine 42, 44, 369
 Fludrocortisone 214
 Flunarizine 236
 Fluorescein Sodium 438
 Fluoxetine 317
 Flupenthixol Decanoate 309
 Fluphenazine Hydrochloride 307
 Flurazepam Monohydrochloride 323
 Fluromethalone 436
 Flutamide 223, 419
 Fluticasone propionate 177
 Foam surgical dressings 381
 Folic acid 114
 Follicle stimulating hormone (FSH) – Urofollitropin 202
 Formaldehyde 381
 Forscarnet 20, 432
 Framycetin Sulphate 361
 Frusemide (furosemide) 143, 333, 397
 Furazolidone 387
 Fusidic Acid 35, 361
 Gabapentin 289
 Gamma benzene hexachloride 379, 380
 Ganciclovir 48, 50, 371
 Gemfibrosil 140
 Gentamicin 18, 69, 71, 385, 423, 432
 Gentian Violet 368
 Giriseofulvin 369
 Glibenclamide (Gliburide) 191
 Gliclazide 192
 Glipizide 192
 Glucagon 198
 Glucocorticoids 213, 214

Glutaraldehyde 381
 Glycerine 89, 519
 Glyceryl Trinitrate 131
 Glycopyrrolate 355, 381
 Glycopyrronium Bromide 355
 Gold 347
 Gold salts 376
 Gonadorelin - (GnRH) 199
 Gonadorelin analogues 200
 Gonadotrophins 202, 406
 Griseofulvin 42, 44, 377
 Growth Hormone (GH) – Somatropin 203
 Growth Hormone Releasing Hormones (GHRH) 200
 Guaiphenesin 183
 Guar gum 193
 Haematopoietic growth factors 265
 Haemocoagulase 187
 Haemostatics 187
 Halofantrine 53, 57, 58
 Haloperidol 298, 309
 Haloprogyn 42, 366
 Halothane 352
 Hamycin 42, 44
 Heavy metals 347
 Heparin 137, 188, 272
 Homatropine 437
 Human Chorionic Gonadotropin (HCG) 202
 Human interferons 49
 Human Menopausal Gonadotropins 203
 Hyaluronidase 250
 Hydralazine 152
 Hydrochlorothiazide 142, 330, 397
 Hydrocolloid dressings 381
 Hydrocortisone 176, 213, 214, 243, 436
 Hydroflumethiazide 332
 Hydrogel dressings 381
 Hydroxy chloroquine 53
 Hydroxy Ethyl Theophylline (Deriphylline) 393
 Hydroxy progesterone caproate 418
 Hydroxy stilbamidine 59
 Hydroxy Urea 261, 420
 1, 25 hydroxy Vitamin D 107
 Hydroxymethyl progesterone 436
 Hydroxyprogesterone 220
 Hydroxyzine 429
 Hyoscine butyl bromide 79, 391

Hyoscine Hydrobromide 303, 356
 Hypnotics 439
 Ibuprofen 238, 390
 Idoxuridine 370, 432
 Ifosfamide 410
 Imipramine Hydrochloride 315, 344
 Indapamide 142, 331, 341
 Indomethacin 240
 Injectable contraceptives 405
 Inosiplex 379
 Insulins 194
 Interferon 52
 Interferon Alpha - 2A 420
 Interferon Alpha 262
 Interferon Beta 262
 Intravenous immunoglobulin (i.v. Ig) 267
 Intravenous nitroglycerine 133
 Iodides 208
 Iodine 120
 Ipecacuanha 183
 Ipratropium Bromide 174, 394
 Iron 118
 Isoflurane 353
 Isoflurophate 434
 Isoniazid 165, 389
 Isoprenaline (Isoproterenol) 130
 Isopropamide 81
 Isosorbide 5 mononitrate 132
 Isosorbide Dinitrate 132
 Ispaghula husk 90
 Itraconazole 42, 47, 71, 72, 369
 Ivermectin 66, 68
 Kanamycin 18, 169, 385
 Ketamine 351
 Ketoconazole 42, 46, 59, 60, 71, 366, 369, 434
 Ketoprofen 239
 Ketotifen 164, 178, 376, 394
 Labetalol 147
 Lactic acid 370
 Lactobacillus Acidophilus 86
 Lactulose 89
 Lamivudine 48
 Lamotrigine 289
 Lansoprazole 77
 L-Asparaginase 420
 Lead 347

Levamisole 65, 68, 387
Levobutanol 436
Levodopa 293
Lignocaine 125, 358
Lincomycin 33
Lincosamide 164
Liquid paraffin 89
Lisinopril 157
Lithium Carbonate 318
Lomefloxacin 32
Loperamide 85
Loratidine 163, 393, 429
Lorazepam 321, 395
Losartan 157
Lovastatin 140
Loxapine 310
Lypressin 205
Macrolides 23, 164, 171
Magnesium carbonate 73
Magnesium hydroxide 73
Magnesium Salts 90
Magnesium trisilicate 73
Magnesium 117
Male sex hormones 221
Mannitol 336, 518, 523
Mebendazole 64, 68, 387
Mebeverine 83
Mechlorethamine (mustine hydrochloride) 407
Medroxy progesterone acetate 220, 418
Mefenamic Acid 240, 390
Mefloquine 53, 56, 58, 59
Megesterol acetate 418
Meglumine 59
Melphalan 265, 381, 408
Meningitis 70
Mepivacaine 359
Mercaptopropionyl glycine 342
Mercaptopurine 411
Mercury 347
Mestamine or mesalazine 93
Mesterolone 222
Methacholine 434
Methadone 183
Methdilazine 429
Methenamine 381
Methicillin 10

Methocarbamol 281
 Methohexitone sodium 350
 Methotrexate 94, 247, 373, 376, 410
 Methyl alcohol 439
 Methyi Cellulose 88
 Methyl Ergometrine 402
 Methyl phenidate 327
 Methyl Prednisolone 213, 337
 Metoclopramide 80, 92, 302, 392
 Metolazone 332
 Metoprolol 146
 Metronidazole 61, 63, 68, 70, 78, 364, 377, 387, 425
 Metyrapone 216
 Mexiletine 125
 Mezlocillin 13
 Mianserin Hydrochloride 316
 Miconazole 42, 45, 368, 433
 Midazolam 396
 Milrinone 129
 Mineralocorticoid 214
 Minocycline 362
 Minoxidil 152, 378
 Mithramycin (plicamycin) 212, 416
 Mitomycin 416
 Mitotane 215, 420
 Mitozantrone 420
 Monochloroacetic acid 370
 Morphine 182, 228, 396
 Mupirocin 37, 360
 Nabilone 84
 Nadroparine 138
 Nafcillin 10
 Naftifine 42, 366
 Nalidixic Acid 33, 71, 387, 526
 Naloxone 327
 Naltrexone 326
 Nandrolone 223, 256
 Naphazoline 159, 421
 Naproxen 238
 Nedocromil sodium 178
 Nefopam Hydrochloride 227
 Neomycin 20, 361
 Neomycin + Polymyxin B + Gramicidin 432
 Neostigmine 278
 Neostigmine 434
 Netilmicin 19, 385

Neutral phosphate 341
 Niacin 111
 Niclosamide 67, 68
 Nicorandil 134
 Nicotinamide 111
 Nicotinic Acid 111, 141
 Nifedipine 149, 319, 397
 Nimesulide 242, 391
 Nimodipine 151
 Niridazole 67, 68
 Nitrates 131
 Nitrazepam 323
 Nitrofuramkin 69
 Nitrofurantoin 36, 523
 Nitrogen mustards 407
 Nitrous Oxide 354
 Nizatidine 76
 Non-Opioid Analgesics 225
 Norethisterone 220
 Norfloxacin 30, 71, 423, 432
 Nortriptyline Hydrochloride 316
 NSAIDs 227, 236, 347, 440
 Nystatin 42, 43, 72, 369, 433
 Oestradiol 218, 219
 Oestriol 218, 219
 Oestrogens 217
 Ofloxacin 31, 71
 Oleandomycin 26
 Omeprazole 76
 Ondansetron 83
 Opioid Analgesics 227
 Oral contraceptives 405
 Orphenadrine Hydrochloride 297
 Orthophosphate 342
 Oxazepam 321
 Oxiconazole 366
 Oxybutinine 344
 Oxygen therapy 185
 Oxymetazoline 159, 421
 Oxymethelone 256
 Oxyrocics 401
 Oxytetracycline 22, 432
 Oxytocin 401, 403
 Paclitaxel 420
 Pancuronium Bromide 356
 Pantothenic acid 112

Para Aminosalicyclic Acid (PAS) 171, 390
 Paracetamol 226, 238, 390
 Paraldehyde 395
 Paramethasone 213
 Parenteral nutritions 122
 Parnaparine 138
 Paromomycin 21
 Pefloxacin 31
 Pemoline 328
 Penciclovir 48
 Penicillamine 245, 342
 Penicillin G 7, 69, 70, 432
 Penicillin V 7, 69, 386
 Penicillins - Broad spectrum 10
 Penicillins - Extended spectrum 12
 Penicillins - betalactamase resistant 9
 Penicillins 7, 69, 164, 363, 386
 Pentamidine 59, 60, 71
 Pentazocine 396
 Pentazocine Hydrochloride 231
 Perindopril 157
 Permethrin 379, 380
 Pethidine 232, 396
 Phenindione 139, 274
 Pheniramine Maleate 392, 429
 Phenobarbitone 284, 395
 Phenol 370
 Phenothiazines 305
 Phenoxymethyl penicillin 7
 Phenylephrine 160, 421, 437
 Phenytoin 125, 285, 439
 Pholcodeine 182
 Physostigmine 434
 Pilocarpine 434
 Pimozide 310
 Piperacillin 13
 Piperazine 65, 68, 387
 Piroxicam 241
 Plicamycin 212
 Podophyllum resin 370
 Polyene Antibiotics 28
 Polymyxin - B 29, 361
 Polythiazide 332
 Polyurethane dressings 381
 Posterior pituitary hormones 203
 Potassium citrate 341, 344

Potassium iodide 183
Potassium permanganate 375
Potassium 116
Povidine iodine 64, 425
Praziquantel 67, 68
Prazosin 154, 342
Precipitated sulphur 380
Prednisolone 175, 213, 252, 266, 337, 436
Prednisone 213
Prepared C1 inhibitor concentrate 376
Prilocaine 359
Primaquine 53, 55, 58, 59, 388
Primidone 285, 298
Probenecid 250
Procainamide 124
Procaine penicillin 7
Procaine 359
Procarbazine 266, 410
Prochlorperazine 84, 301, 308
Procyclidine 327
Procyclidine Hydrochloride 297
Progesterone 220
Progestogens 219
Proguanil 53, 54, 58, 59
Promethazine 85, 299, 325, 391, 396, 429
Propantheline bromide 93, 344
Propofol 352
Propranalol 145, 298, 327, 397,
Propyl thiouracil 207
Prostaglandin 402, 403
Protamine sulphate 273
Proteins 102
Prothionamide 42, 170
Protirelin 200
Protriptyline 181
Pseudomonic acid 37
Psoralen with UVA therapy (PUVA) 373, 378
Pyrantel pamoate 65, 68, 387
Pyrazinamide (PZA) 166, 390
Pyridostigmine Bromide 279
Pyridoxine 111, 341
Pyrimethamine 53, 54, 58, 388
Quinidine 53, 57, 123, 439
Quinine 53, 55, 57, 388
Quinolones 30, 164, 171, 346
Radiocontrast media 346

Ramipril 157
 Ranitidine 75
 Reserpine 154
 Resorcinol 377
 Retinoids 374, 376
 Ribavirin 49, 52
 Riboflavin 110
 Rifampicin 41, 69, 70, 165, 364, 389
 Rimantadine 49, 51
 Risperidone 311
 Ropivacaine 359
 Roxatidine 76
 Roxithromycin 27, 364
 Rubefacients 251
 Rutin 187
 Salbutamol 172, 393
 Salicylazosulphapyridine 37
 Salicylic acid 370, 371
 Salmeterol 173
 Scopolamine hydrobromide 381
 Secnidazole 61
 Selegiline 296
 Senna 88
 Sermorelin, Somatostatin 200
 Sertraline 318
 Sex hormones 216
 Silver-sulphadiazine 38
 Simethicone 91
 Simvastatin 140
 Sisomicin 361
 Skeletal Muscle Relaxants 279
 Sodium Aurothiomalate 244
 Sodium bicarbonate 73, 344, 424
 Sodium Chloride 116, 160
 Sodium citrate 344
 Sodium cromoglycate 161, 177, 394, 422
 Sodium Etidronate 212
 Sodium Nitroprusside 152
 Sodium Stibogluconate 59, 60
 Sodium Thiosulphate 368
 Sodium valproate 286, 319, 395
 Sodium/potassium acetate 183
 Sotalol 127, 146
 Sparfloxacin 32
 Spectinomycin 36, 69
 Spiramycin 27

Spironolactone 144, 335, 397
Stanozolol 224
Stavudine 48
Stilboestrol 417
Streptokinase 34, 276
Streptomycin 17, 167, 390
Succinyl sulphathiazole 37
Sulconazole 367
Sulfadiazine 386
Sulfapyridine 376
Sulfonamides 346
Sulfoxone Sodium 41
Sulphacetamide 37, 432
Sulphadiazine 37
Sulphadimidine 37
Sulphadoxine 37, 53
Sulphaguanidine 37
Sulphamethoxazole 37, 38, 70
Sulphamethoxy pyridazine 37
Sulphametopyrazine 37
Sulphasalazine 37, 93
Sulphonamides 37
Sulphonyl Ureas 190
Sulphur 377
Sumatriptan 234
Survanta 185
Sustained Release Theophyllin 394
Suxamethonium Chloride 357
Systemic corticosteroids 376
Talampicillin 12
Tamoxifen 419
Teicoplanin 35
Tenoxicam 242
Terazosin 155, 342
Terbinafine 42, 48, 367, 369
Terbutaline 172, 393
Terfenadine 162, 430
Terlipressin 205
Testosterone 221
Tetracosactrin 202
Tetracycline 21, 58, 164, 346, 362, 377, 432
Theophylline 174, 181
Thiabendazole 66, 68
Thiamine 109
Thiazide diuretics 340
6-Thioguanine 412

Thiopentone sodium 350
 Thioridazine Hydrochloride 307
 Thymol 367
 Thyroid Hormone 205
 Thyrotropin releasing hormone (TRH) 200
 Thyroxine Sodium (T₄) 206
 Tibolone 219
 Ticarcillin 12
 Ticlopidine 137, 271
 Timolol 435
 Tinidazole 61, 63, 64, 79, 387
 Tinzaparine 138
 Tissue Plasminogen Activator (Alteplase) tPA 135, 277
 Tobramycin 19, 432
 Tobramycin 71
 Tolanaftate 42
 Tolbutamide 190
 Tolnaftate 368
 Topical antibiotics 377
 Topical counter irritants 251
 Topical Steroids 372
 Torasemide 335
 Tramadol Hydrochloride 232
 Tranexamic acid 275, 376
 Tranquilizers 439
 Trazodone Hydrochloride 317
 Tretinoin 370, 377
 Triamcinolone 213, 243, 252, 437
 Triamterene 144, 335
 Trichloroacetic acid 370
 Triclofos 324, 396
 Tricyclic antidepressants 235
 Trifluoperazine 301
 Trifluoperazine Hydrochloride 307
 Trifluridine 72, 433
 Trihexyphenidyl (benzhexol) 327
 Tri-iodo-thyronine (T₃) 206
 Trimeprazine tartarate 396
 Trimetazidine 133
 Trimethoprim - Sulfamethoxazole 38, 69, 70, 71, 363
 Trimipramine Maleate 316
 Triprolidine 430
 Tropicamide 437
 Ulcer healing drugs 74
 Undecenoic acid 369
 Undecylenic acid 42

Urea stibamine 59
 Urokinase 135, 277
 Ursodeoxycholic acid 95
 Vaccines 466 - 478
 Valacyclovir 48
 Vancomycin 34, 69, 70, 164
 Vasaka 183
 Vasopressin 204
 Vecuronium Bromide 357
 Verapamil 48, 319
 Vesnarinone 129
 Vigabatrin 287
 Vinblastine 413
 Vincristine 266, 268, 414
 Vitamin A 105
 Vitamin B12 112
 Vitamin B2 110
 Vitamin B3 111
 Vitamin B6 111
 Vitamin C 114
 Vitamin D Derivatives 211
 Vitamin D 106
 Vitamin E 108
 Vitamin K - coagulation vitamin 108
 Vitamins - water soluble 108
 Vitamins B1 109
 Vitamins - Fat soluble 105
 Vitamins 105
 Warfarin 138
 Warts 370
 Wet compresses 376
 Whitfield's Ointment 367
 Xipamide 142, 332
 Xylocaine 434
 Xylometazoline 159, 421
 Zafirlukast 179
 Zalcitabine 48
 Zidovudine 48, 50, 72, 347
 Ziluton 179
 Zinc oxide 381
 Zopiclone 324

REPORT ON SUSPECTED ADVERSE DRUG REACTIONS

- Recently introduced products

Please report all suspected reactions, including minor ones that could conceivably be attributed to the drug.

- Please also report reactions to vaccines
- Record all other drugs taken in previous 3 months including self-medication.
- Report suspected drug interactions.

Established products

Please report serious or unusual suspected reactions to all agents but not minor reactions, include reactions that are fatal, life-threatening, disabling incapacitating, or which result in or prolong hospitalisation.

Do not be put off reporting because some details are not known

REPORTING DOCTOR

Name and Professional Address _____

Telephone _____ Speciality _____

Signature _____ Date _____

PATIENT'S DETAILS

Name _____ Other Names _____

Date of birth (or age) _____ Sex: ☐ M ☐ F Weight (kg) _____

Hospital if relevant _____ Hospital Number _____

Consultant in charge or GP Principal _____

SUSPECTED DRUG

Give brand name of drug and batch number if known _____ Daily dose _____ Date drug started _____ Date drug stopped _____ Therapeutic indication _____

SUSPECTED REACTIONS

Was the patient hospitalised because of the reaction?

Yes ☐ No ☐

Date reaction started _____ Date reaction ended _____ Outcome (eg. fatal, recovered, continuing) _____

KSDF

ADVERSE REACTIONS

Blue forms are included in the KSDF.

Please report suspected reactions to:

Kerala State Drug Formulary Committee

College of Pharmaceutical Sciences

Medical College

Thiruvananthapuram 695 011, Kerala, India.